Please see Prescribing Information for full details about the risks of ZYPREXA RELPREVY, including Boxed Warnings.
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**Introduction to the ZYPREXA RELPREVV Patient Care Program**

**Patient Care Program Overview**
ZYPREXA RELPREVV is the long-acting intramuscular formulation of olanzapine indicated for treatment of schizophrenia. The ZYPREXA RELPREVV Patient Care Program is a Risk Evaluation and Mitigation Strategy (REMS) program necessary to mitigate the risk of negative outcomes associated with ZYPREXA RELPREVV post-injection delirium/sedation syndrome (PDSS). In order to prescribe, dispense, receive, or administer ZYPREXA RELPREVV, healthcare professionals need to:

- Enroll in the ZYPREXA RELPREVV Patient Care Program
- Ensure the collection of information for each injection of ZYPREXA RELPREVV

**Post-Injection Delirium/Sedation Syndrome:**
ZYPREXA RELPREVV has been associated with a post-injection delirium/sedation syndrome characterized primarily by signs and symptoms consistent with olanzapine overdose. This syndrome does not apply to any other formulation of olanzapine, including ZYPREXA IntraMuscular (olanzapine for injection). The prescribing information for ZYPREXA RELPREVV includes the following BOXED WARNING.

**BOXED WARNING**

See full prescribing information and the healthcare professional training for complete information on PDSS.

Post-Injection Delirium/Sedation Syndrome — Adverse events with signs and symptoms consistent with olanzapine overdose, in particular, sedation (including coma) and/or delirium, have been reported following injections of ZYPREXA RELPREVV. ZYPREXA RELPREVV must be administered in a registered healthcare facility with ready access to emergency response services. After each injection, patients must be observed at the healthcare facility by a healthcare professional for at least 3 hours. Because of this risk, ZYPREXA RELPREVV is available only through a restricted distribution program called ZYPREXA RELPREVV Patient Care Program and requires prescriber, healthcare facility, patient, and pharmacy enrollment.

Increased Mortality in Elderly Patients with Dementia-Related Psychosis — Elderly patients with dementia related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear. ZYPREXA RELPREVV is not approved for the treatment of patients with dementia-related psychosis.
For questions regarding the Patient Care Program or to enroll, please contact the Patient Care Program Coordinating Center:

**Via Telephone:** 1-877-772-9390  
Monday – Friday: 8:00am – 8:00pm ET

**Via Mail:** ZYPREXA RELPREVV Patient Care Program  
P.O. Box 4649  
Star City, WV 26504-4649

**Via Fax:** 1-877-772-9391

**Via Internet:** [www.zyprexarelprevvprogram.com](http://www.zyprexarelprevvprogram.com)
Prescriber Information

Prescribers must enroll in the ZYPREXA RELPREVV Patient Care Program in order to prescribe ZYPREXA RELPREVV.

Enrolling in the ZYPREXA RELPREVV Patient Care Program will allow prescribers to securely and easily view data for all of the patients they have enrolled in the program, along with the patients' next expected injection dates and injection histories.

Upon registration, the prescriber will be sent a username and password, which allows secured access to the on-line Patient Care Program system. The prescriber is responsible for entering required Patient Care Program data for any PDSS event that occurs.

Prescribers who obtain ZYPREXA RELPREVV through a pharmacy: Provide a prescription to a registered pharmacy.

Prescribers who order and dispense ZYPREXA RELPREVV through buy and bill procedures: Enroll as a Buy and Bill Pharmacy Service Provider as described on pages 9 and 10 of this brochure.

The facility/practice where injections are administered or patients are monitored must be enrolled in the ZYPREXA RELPREVV Patient Care Program as a healthcare facility as described on page 7. The Prescriber will receive an email or fax notification once the healthcare facility(s) become enrolled. The healthcare facility(s) are required to enter data following each patient injection.

Three Steps to Prescriber Enrollment:

1. **Review:**
   - Attend a training or review the following educational materials:
     - ZYPREXA RELPREVV Patient Care Program Instructions Brochure (this document)
     - Healthcare Professional Training Slide Presentation with text notes or Recorded Presentation with participant guide, available at www.zyprexarelprevprogram.com

2. **Complete/Sign:**
   - Complete the Prescriber Registration Form on-line, or print and sign.

3. **Submit:**
   - Submit on-line or via fax or mail to the Patient Care Program Coordinating Center.

Prescribers must repeat the enrollment process every 3 years. You will be notified by fax or email 60 days prior to your reenrollment date.
Prescriber Information

To report SUSPECTED ADVERSE REACTIONS other than PDSS, contact Eli Lilly and Company at 1-800-LILLYRX (1-800-545-5979) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

The prescriber is responsible for enrolling the patient in the ZYPREXA RELPREVV Patient Care Program prior to writing a prescription for that patient.

Three Steps to Patient Enrollment:

1. Confirm:
   • Both the prescriber and the healthcare facility where the patient will receive the injection are enrolled in the ZYPREXA RELPREVV Patient Care Program.
   • Patient has been provided with a Medication Guide and informed about the risks associated with the administration of ZYPREXA RELPREVV.
   • Patient has been informed about the Patient Care Program guidelines.

2. Complete/Sign:
   Complete a Patient Registration Form and have the patient or legal guardian sign the form, or check the box relating to the presence of a court order. If the court order box is checked, provide the expiration date of the court order. Provide the Patient Registration Form-Patient Copy version to the patient or legal guardian.

3. Submit:
   Submit on-line or via fax or mail to the Patient Care Program Coordinating Center.

For any changes in patient care setting, changes in prescriber, or to discontinue or reactivate a patient, call the Coordinating Center (1-877-772-9390).

Patient Care Program Data Entry
All suspected cases of PDSS should be reported to the ZYPREXA RELPREVV Patient Care Program within 24 hours of awareness of the event. The ZYPREXA RELPREVV Patient Care Program may need to contact you to obtain additional information to further characterize the PDSS event.

For each suspected PDSS event, the prescriber can record and submit data to the Patient Care Program in one of the following ways:

Via Telephone: 1-877-772-9390
Via Fax: 1-877-772-9391
Via Internet: www.zyprexaelprevvprogram.com

Steps for On-line Data Entry

1. With the assigned username and password, log in to the ZYPREXA RELPREVV Patient Care Program system through the website.

2. Upon logging into the Patient Care Program system, the prescriber will see only their associated patients and the option to enroll new patients.

3. Select:
   • The appropriate patient for whom he/she is entering data.
   • Or the option to enroll a new patient.

4. The system will prompt the prescriber to enter enrollment data for a new patient, or PDSS data for an already enrolled patient.

After enrollment is complete, a unique Patient Identification Number (PIN) and a healthcare facility unique identifier will be provided to the prescriber via a patient authorization notification fax or email.

The prescriber should provide the patient’s PIN and healthcare facility unique identifier with the first prescription to assist the pharmacy service provider in completing its ZYPREXA RELPREVV Patient Care Program responsibilities.
Healthcare Facility Information

A healthcare facility must be enrolled in the ZYPREXA RELPREVV Patient Care Program to: ensure each patient is enrolled in the Patient Care Program prior to administering an injection, to administer ZYPREXA RELPREVV and/or to monitor patients who have been administered ZYPREXA RELPREVV and to enter data for each injection administered to a patient.

Authorized Healthcare Facility Representative

The authorized healthcare facility representative must ensure that all appropriate staff responsible for administering ZYPREXA RELPREVV and for monitoring patients are educated on ZYPREXA RELPREVV injection techniques, signs and symptoms of PDSS, and patient monitoring requirements following injection. Additionally, the authorized healthcare facility representative is responsible to ensure systems are in place to report all PDSS events to the prescriber and to identify all appropriate staff as delegates who will be responsible for entering data following each injection.

Patient Care Program Data Entry

The authorized healthcare facility representative may assign the Patient Care Program responsibilities to a delegate(s). Upon registration, the delegate(s) will be sent a username and password, which allows secured access to the on-line Patient Care Program system. After registration, additional delegates may be assigned by calling the Coordinating Center (1-877-772-9390).

Three Steps to Healthcare Facility Enrollment:

1. **Review:**
   Staff involved with ZYPREXA RELPREVV patients review the educational materials listed below. Materials are available on-line, through an on-line order form, or by calling the ZYPREXA RELPREVV Patient Care Program Coordinating Center.
   
   - Required for nurse or other individuals giving injections:
     - ZYPREXA RELPREVV Patient Care Program Instructions Brochure (this document)
     - Healthcare Professional Training Slide Presentation with text notes or Recorded Presentation
     - Reconstitution & Administration Training Video and Poster

   - Required for staff working with patients post-injection:
     - Healthcare Professional Training Slide Presentation with text notes or Recorded Presentation
     - ZYPREXA RELPREVV Patient Care Program Instructions Brochure (this document)

2. **Complete/Sign:**
   Healthcare facility representative completes the Healthcare Registration Form on-line or print and sign.

3. **Submit:**
   Submit on-line or via fax or mail to the ZYPREXA RELPREVV Patient Care Program Coordinating Center.

Healthcare facilities must repeat the enrollment process every 3 years. You will be notified by fax or email 60 days prior to your reenrollment date.
Healthcare Facility Information

After a patient associated with your facility is enrolled by a prescriber, a unique Patient Identification Number (PIN) will be assigned to the patient and provided to the facility via a patient authorization notification fax or email, which should be filed in the patient’s chart.

Prior to each injection, verify that the patient is enrolled in the Zyprexa Relprevv Patient Care Program registry by accessing the system.

Following the injection, patients are to be monitored continuously for at least 3 hours. Report required Patient Care Program injection data (see Injection Form) **within 7 days of injection administration.**

Injection data may be submitted individually for each patient by using the Single Patient Injection Form or for multiple patients by using the Multiple Patient Injection Form.

For each injection, record and submit injection data to the Patient Care Program in one of the following ways:

**Via Telephone:** 1-877-772-9390

**Via Fax:** 1-877-772-9391

**Via Internet:** www.zyprarelprevvprogram.com

**Steps for On-line Data Entry**

1. With the assigned username and password, log in to the ZYPREXA RELPREVV Patient Care Program system through the website.
2. Upon logging into the Patient Care Program system, the delegate will see only their associated patients.
3. Select the appropriate patient and dispense date to enter injection data.
4. The system will prompt the delegate to enter injection data for an enrolled patient.

**Product Replacement**

If, during the course of reconstitution or administration of ZYPREXA RELPREVV, the medication becomes unusable (e.g., aspiration of blood or a broken vial), call the Coordinating Center.
Pharmacy Service Provider Information

A pharmacy service provider must be enrolled in the ZYPREXA RELPREVV Patient Care Program to order and dispense ZYPREXA RELPREVV. Pharmacy service providers include any retail pharmacy, hospital pharmacy, physician or healthcare facility that can order and dispense ZYPREXA RELPREVV.

Three Steps to Pharmacy Service Provider Enrollment:

1. **Review:**
   Pharmacy staff should review the training and education material within this document before dispensing the medication.

2. **Complete:**
   Representative for the pharmacy service provider completes a registration form, depending upon the type of pharmacy operation.
   - **Pharmacy Registration Form:** Enrolls a pharmacy to allow ordering and dispensing of ZYPREXA RELPREVV. To be completed by the pharmacist in charge.
   - **Buy and Bill Pharmacy Service Provider Registration Form:** Enrolls a prescriber organization that wishes to order and dispense ZYPREXA RELPREVV to patients through buy and bill procedures.

3. **Submit:**
   Submit on-line or via fax or mail to the ZYPREXA RELPREVV Patient Care Program Coordinating Center.

Pharmacy Service Providers must repeat the enrollment process every 3 years. You will be notified by fax or email 60 days prior to your reenrollment date.

Ordering ZYPREXA RELPREVV

ZYPREXA RELPREVV will be shipped through a controlled distribution system. Following the pharmacy service provider registration, the Patient Care Program Coordinating Center will notify distributors that the pharmacy is enrolled. The pharmacy will then be able to submit orders for ZYPREXA RELPREVV to their regular wholesaler.

Patient Care Program requirements must be followed for the pharmacy to maintain an active registration status and to have continued access to ZYPREXA RELPREVV.

Dispensing ZYPREXA RELPREVV

It is the responsibility of the pharmacy service provider to verify the ongoing eligibility of the patient prior to dispensing each prescription and entering the date of each dispensing. The pharmacist will ensure prescription verification (including patient eligibility check and recording the dispense date) is completed on the date of dispense, prior to the convenience kit leaving the pharmacy. This is accomplished by contacting the Patient Care Program in one of the following ways:

**Via Telephone/IVRS:** 1-877-772-9390

**Via Internet:** www.zyprexa-relpervvprogram.com

Prior to dispensing ZYPREXA RELPREVV, the pharmacy service provider must confirm that the prescriber, healthcare facility, and patient are enrolled in the ZYPREXA RELPREVV Patient Care Program and that the patient is eligible to receive ZYPREXA RELPREVV via the process outlined below. The pharmacy service provider must only dispense ZYPREXA RELPREVV to registered healthcare facilities or a healthcare professional, not directly to a patient.

A patient identification number (PIN) and healthcare facility unique identifier should be provided by the prescriber with the first prescription. Through the on-line Patient Care Program system, the PIN will quickly identify the patient and prescriber as enrolled in the Patient Care Program. The healthcare facility unique identifier will allow confirmation of healthcare facility registration. The system will indicate the patient’s eligibility to receive a dispensing of ZYPREXA RELPREVV.

Once the ZYPREXA RELPREVV Patient Care Program Coordinating Center receives the completed registration form, the pharmacy service provider will be sent a username and password, which allows secured access to the on-line Patient Care Program system and interactive voice response system (IVRS).

Reference ID: 3675779
Patient eligibility is determined by enrollment in the Patient Care Program and entry of required injection data into the Patient Care Program system by the healthcare facility.

**Steps to Dispense:**

1. Order the product from a distributor.

2. Receive ZYPREXA RELPREVV from distributor and maintain a supply of product at the pharmacy.

3. Receive a valid prescription, patient identification number (PIN), and healthcare facility unique identifier.

4. Maintain the PIN and healthcare facility unique identifier in the patient record within the pharmacy system to access when refilling a prescription.

5. With the assigned username and password, access the ZYPREXA RELPREVV Patient Care Program system in one of three ways: access the website or call the Coordinating Center (1-877-772-9390) and chose either the Interactive Voice Response System (IVRS) option or speak to a Patient Care Program representative.

**Web based – www.zyprexarelprevvprogram.com**

- Enter the PIN (If the PIN is not provided, call the Coordinating Center and provide patient’s first and last name, patient’s date of birth and prescriber’s name).
  - System displays prescriber and patient name
  - Confirm both names match prescription
  - System displays healthcare facility number and name
  - Confirm healthcare facility name/unique identifier matches patient authorization notification
  - The system will indicate the patient’s eligibility to receive ZYPREXA RELPREVV.

- If eligible, the pharmacist will enter the date of dispensing (prior to the convenience kit leaving the pharmacy) into the Patient Care Program system and dispense only to the healthcare facility (representative) associated with that patient. Do NOT dispense directly to a patient.

- If ineligible, do NOT dispense product. Contact the Patient Care Program Coordinating Center for resolution.

**Interactive Voice Response System – call 1-877-772-9390**

- Enter the PIN (If the PIN is not provided, call the Coordinating Center and provide patient’s first and last name, patient’s date of birth and prescriber’s name).
  - IVRS provides first 5 letters of prescriber and patient last name
  - Confirm both names match prescription
  - IVRS provides healthcare facility unique identifier
  - Confirm unique identifier/healthcare facility name matches patient authorization notification
  - The system will indicate the patient’s eligibility to receive ZYPREXA RELPREVV.

- If eligible, the pharmacist will enter the date of dispensing (prior to the convenience kit leaving the pharmacy) into the Patient Care Program system and dispense only to the healthcare facility (representative) associated with that patient. Do NOT dispense directly to a patient.

- If ineligible, do NOT dispense product. Contact the Patient Care Program Coordinating Center for resolution.
Pharmacy Service Provider Information

Call the Coordinating Center Help Desk
1-877-772-9390

• Provide the PIN (If the PIN is not available, provide patient’s first and last name, patient’s date of birth and prescriber’s name).

• Patient Care Program representative will ask pharmacy provider questions and provides verification of patient eligibility to receive ZYPREXA RELPREVV.

• If eligible, Patient Care Program representative will enter the date of dispensing prior to the convenience kit leaving the pharmacy.

• Pharmacy Service Provider agrees to dispense only to the healthcare facility (representative) associated with that patient and not directly to a patient.

• If ineligible, Do NOT dispense product. The Coordinating Center will work to resolve.

Product Replacement

If, during the course of administering a ZYPREXA RELPREVV injection to a patient, an accident occurs that causes the ZYPREXA RELPREVV vial to be broken or to become unusable (e.g., aspiration of blood), call the Coordinating Center.

Reconciliation

Shipping records will be monitored against dispensing data by the Patient Care Program. If dispensing data are not provided, the pharmacy service provider will be contacted to obtain the information. Unreconciled discrepancies may lead to removal of the pharmacy from the approved list of pharmacies for ZYPREXA RELPREVV.
Glossary of Terms

Healthcare Facility
A healthcare facility administering and/or monitoring injections of ZYPREXA RELPREVV.

Interactive Voice Response System (IVRS)
System that allows a pharmacy service provider to confirm patient and prescriber eligibility and provide dispensing data via telephone rather than the on-line system.

Patient Authorization Notification
Provided to the prescriber and healthcare facility upon registration and includes the PIN and healthcare facility unique identifier. To be provided to the pharmacy service provider with the first prescription for each patient.

Patient Identification Numbers (PIN)
Unique numbers assigned to patients, which are used by the pharmacy service provider to confirm enrollment in the ZYPREXA RELPREVV Patient Care Program.

Pharmacy Service Provider
Any retail pharmacy, hospital pharmacy, physician, or properly licensed healthcare facility that can order for and deliver ZYPREXA RELPREVV to a healthcare professional in accordance with their agreement to implement all relevant requirements of the ZYPREXA RELPREVV Patient Care Program.

- Pharmacy - Retail and hospital pharmacies
- Buy & Bill Pharmacy Service Provider – a licensed healthcare provider that purchases pharmaceuticals through a licensed distributor for its own use in the treatment of a patient and then includes the cost of the pharmaceutical in its billing of patients and third-party payers.

Post-Injection Delirium/Sedation Syndrome (PDSS)
During premarketing clinical studies, adverse events that presented with signs and symptoms consistent with olanzapine overdose, in particular, sedation (including coma) and/or delirium, were reported in patients following an injection of ZYPREXA RELPREVV. Sedation ranged from mild in severity to coma and delirium included confusion, disorientation, agitation, anxiety, and other cognitive impairment. Other symptoms noted include extrapyramidal symptoms, dysarthria, ataxia, aggression, dizziness, weakness, hypertension, and convulsion. The potential for onset of the event is greatest within the first hour. The majority of cases have occurred within the first 3 hours after injection; however, the event has occurred after 3 hours.

Prescriber
A healthcare professional writing prescriptions for ZYPREXA RELPREVV. Prescribers are responsible for ensuring that all patients receiving ZYPREXA RELPREVV are enrolled in the program.
BUY & BILL® PHARMACY SERVICE PROVIDER REGISTRATION FORM

To be enrolled in the ZYPREXA RELPREVX Patient Care Program, complete and fax this form to 1-877-772-9391.

Training must be completed before a pharmacy service provider may be enrolled in the ZYPREXA RELPREVX Patient Care Program.

PHARMACY SERVICE PROVIDER INFORMATION

☐ Enrollment  ☐ Reenrollment

Facility Name: ________________________________

DEA Number: ________________________________

Please specify description of Pharmacy: ☐ Community/Retail  ☐ Specialty Pharmacy  ☐ Hospital or Institution  ☐ Other

Address Line 1: ________________________________

Address Line 2: ________________________________

City: __________________  State: __________  Zip: __________
Primary Phone: __________________  Secondary Phone: __________________
Fax: __________________

SHIP TO INFORMATION

Ship To Address (if the same as above, check here)  ☐
Ship To Contact Name: __________________________

Address Line 1: ________________________________

Address Line 2: ________________________________

City: __________________  State: __________  Zip: __________
Primary Phone: __________________  Secondary Phone: __________________
Fax: __________________

ADMINISTRATOR INFORMATION

First Name: __________________  Middle Initial: ______  Last Name: __________________

Preferred Method of Communication:  ☐ Email  ☐ Fax

Email: __________________

Phone: __________________  Fax: __________________ (if different from above)

PHARMACY SERVICE PROVIDER AGREEMENT

By signing below, I acknowledge that:

• I have read and understand the ZYPREXA RELPREVX Patient Care Program Instructions Brochure.
• I will ensure that all appropriate pharmacy staff are trained and have read and understand the ZYPREXA RELPREVX Patient Care Program Instructions Brochure.
• I will ensure that all appropriate pharmacy staff understand that ZYPREXA RELPREVX can only be dispensed for use in certain health care settings (e.g., hospitals, clinics) that have ready access to emergency response services and that can allow for continuous patient monitoring for at least 3 hours post-injection.
• I will ensure that pharmacy staff will verify that the patient is enrolled in the ZYPREXA RELPREVX Patient Care Program registry prior to dispensing each prescription/refill by accessing the system.
• I will ensure that pharmacy staff will not dispense ZYPREXA RELPREVX directly to patients.
• I will ensure pharmacy staff report the date of each ZYPREXA RELPREVX dispensing to the ZYPREXA RELPREVX Patient Care Program.
• For each dispensing I will ensure prescription verification (includes patient eligibility check and recording the dispense date) is completed on the date of dispense, prior to the convenience kit leaving the pharmacy.
• I understand that the ZYPREXA RELPREVX Patient Care Program Coordinating Center may contact the pharmacy to clarify information provided or to obtain information about the patient.

I may cancel this registration by notifying the ZYPREXA RELPREVX Patient Care Program Coordinating Center by fax at 1-877-772-9391 or by phone at 1-877-772-9390. If I cancel, Lilly will cease to supply ZYPREXA RELPREVX to the facility.

Administrator Signature: __________________

Date: __________  month  __________  day  __________  year

* Buy & Bill Pharmacy Service Provider - a licensed healthcare provider that purchases pharmaceuticals through a licensed distributor for its own use in the treatment of a patient and then includes the cost of the pharmaceutical in its billing of patients and third-party payers.

PHONE 1-877-772-9390  FAX 1-877-772-9391  www.zyprexaerelprevxprogram.com

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To be enrolled in the ZYPREXA RELPREVV Patient Care Program, complete and fax this form to 1-877-772-9391.
Training must be completed before a healthcare facility may be enrolled in the ZYPREXA RELPREVV Patient Care Program.

HEALTHCARE FACILITY INFORMATION

☐ Enrollment  ☐ Reenrollment

Healthcare Facility Name: ______________________________________________________

Please specify location of Healthcare Facilities:  ☐ Prescriber Office  ☐ Clinic/Outpatient Facility  ☐ Hospital  ☐ Other

Address: ______________________________________________________________________

City: __________________________ State: __________ Zip: __________

Phone: __________________________ Fax: __________________________________

AUTHORIZED HEALTHCARE FACILITY REPRESENTATIVE INFORMATION

First Name: __________________________ Mi: ___ Last Name: __________________________

Position/Title: ___________________________________________________________________

Phone: __________________________ Fax: __________________________________

Email: __________________________

Preferred Method of Communication:  ☐ Email  ☐ Fax

You may identify Delegate(s) to enter the necessary patient data into the Patient Care Program system.

Delegate First Name: __________________________ Mi: ___ Last Name: __________________________

Facility Name: ______________________________________________________________________

Phone: __________________________ Fax: __________________________

Email: __________________________

Delegate First Name: __________________________ Mi: ___ Last Name: __________________________

Facility Name: ______________________________________________________________________

Phone: __________________________ Fax: __________________________

Email: __________________________

Delegate First Name: __________________________ Mi: ___ Last Name: __________________________

Facility Name: ______________________________________________________________________

Phone: __________________________ Fax: __________________________

Email: __________________________

Delegate First Name: __________________________ Mi: ___ Last Name: __________________________

Facility Name: ______________________________________________________________________

Phone: __________________________ Fax: __________________________

Email: __________________________

Delegate First Name: __________________________ Mi: ___ Last Name: __________________________

Facility Name: ______________________________________________________________________

Phone: __________________________ Fax: __________________________

Email: __________________________

If additional Delegates are required contact the Patient Care Program Coordinating Center.

PHONE 1-877-772-9390  FAX 1-877-772-9391  www.zyprexarelprevvprogram.com
HEALTHCARE FACILITY AGREEMENT

As the authorized representative for this facility, I attest that:

- I have read and understand the ZYPREXA RELPREV™ Patient Care Program Instructions Brochure;

- I will ensure that all appropriate staff are trained and have read and understand the ZYPREXA RELPREV™ Patient Care Program Instructions Brochure as well as the following Training Materials:
  - ZYPREXA RELPREV™ Healthcare Professional Training
  - ZYPREXA RELPREV™ Reconstitution and Administration Training

- I will ensure that all appropriate staff understand that ZYPREXA RELPREV™ can only be dispensed for use in certain health care settings (e.g., hospitals, clinics) that have ready access to emergency response services and that can allow for continuous patient monitoring for at least 3 hours post-injection;

- I will ensure the health care setting has systems, protocols, or other measures to ensure that ZYPREXA RELPREV™ is only administered to patients enrolled in the program and that patients are continuously monitored for at least 3 hours post-injection for suspected PDSS;

- I will ensure that appropriate staff will verify that the patient is enrolled in the ZYPREXA RELPREV™ Patient Care Program registry prior to each injection, by accessing the system;

- I will ensure that the Medication Guide is provided to the patient or the patient’s legal guardian prior to each injection;

- I will ensure that the appropriate staff monitors the patient continuously for at least 3 hours;

- I will ensure that required data are submitted within 7 days after each injection to the ZYPREXA RELPREV™ Patient Care Program.

- I understand that the ZYPREXA RELPREV™ Patient Care Program Coordinating Center may contact the health care setting to clarify information provided or to obtain information about the patient.

I confirm that the information above is correct.

I understand that this information will be used to document healthcare facilities that are eligible to administer ZYPREXA RELPREV™.

I also understand that this information may be shared with government agencies.

I understand that Lilly will regularly evaluate ZYPREXA RELPREV™ Patient Care Program compliance to ensure that program objectives are met. Lilly reserves the right to terminate a healthcare facility’s enrollment at any time based upon non-compliance or to take other appropriate measures to assure that the ZYPREXA RELPREV™ Patient Care Program objectives are met.

I may cancel this healthcare facility registration in the future by notifying Lilly in writing and submitting the notification by fax to 1-877-772-9391 or by calling 1-877-772-9390. If I revoke this facility’s registration, the facility will no longer be eligible to administer ZYPREXA RELPREV™ to patients.

Date: [ ] day [ ] month [ ] year

Authorized Healthcare Facility Representative Signature

Authorized Healthcare Facility Representative Name (print) [ ] Title [ ]

Please fax completed form to the ZYPREXA RELPREV™ Patient Care Program at 1-877-772-9391.
MULTIPLE PATIENT INJECTION FORM

IMPORTANT: Before administering the injection, confirm there will be someone to accompany the patient after the 3-hour observation period. If this cannot be confirmed, do not give the injection.
Submit this information within 7 days after the patient's injection. If you are aware that the patient's prescriber has changed, please notify the ZYPREXA RELPREVIV Patient Care Program Coordinating Center.

Injection Facility Name: ____________________________

Date of Injection

<table>
<thead>
<tr>
<th>Month</th>
<th>Day</th>
<th>Year</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient No.: (PIN)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient Name:</td>
<td>First Name</td>
<td>MI</td>
</tr>
<tr>
<td>Date of Birth:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mon h</td>
<td>day</td>
<td>year</td>
</tr>
<tr>
<td>PDSS since last visit? (check one)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>If Yes, has the prescriber been notified of the PDSS event?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Time of Injection (24-hour clock)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose of Injection (check one)</td>
<td>150 mg</td>
<td>210 mg</td>
</tr>
<tr>
<td>300 mg</td>
<td>405 mg</td>
<td>300 mg</td>
</tr>
<tr>
<td>Other dose __________ mg</td>
<td>Other dose __________ mg</td>
<td>Other dose __________ mg</td>
</tr>
<tr>
<td>Observed at least 3 hours post-injection? (check one)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>PDSS during onsite observation? (check one)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>If Yes, has the prescriber been notified of the PDSS event?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Following the injection, was the patient alert, oriented, and absent of any signs and symptoms of PDSS prior to being released from the healthcare facility? (check one)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Following the injection, was the patient accompanied from the facility? (check one)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Signature</td>
<td>Healthcare Facility Staff Member Signature</td>
<td>Healthcare Facility Staff Member Signature</td>
</tr>
<tr>
<td>Healthcare Facility Staff Member Name (print</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date</td>
<td>month</td>
<td>day</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Was the patient or legal guardian given a Medication Guide prior to this injection? | Yes | No | Yes | No | Yes | No |

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Version 2.0 03Aug2012

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Reference ID: 3675779
PATIENT INFORMATION

First Name: _______________________________ MI: ___________________ Last Name: _______________________________

Date: ______________________________

PATIENT AGREEMENT

The maker of ZYPREXA RELPREVY, Eli Lilly and Company and their delegates run the ZYPREXA RELPREVY Patient Care Program.

Your doctor will send your name, date of birth, and other information that directly identifies you to the ZYPREXA RELPREVY Patient Care Program. Ask your doctor if you have questions about the information that will be collected.

The ZYPREXA RELPREVY Patient Care Program will collect and use your information in the following ways:

• Your doctor will provide dose, date and time of each injection, and other medical information to the ZYPREXA RELPREVY Patient Care Program.

• Your information will be stored in the ZYPREXA RELPREVY Patient Care Program computer system.

• The information will be used to help Lilly learn more about the safety of ZYPREXA RELPREVY.

• Information from all patients in the ZYPREXA RELPREVY Patient Care Program will be reviewed and may be combined with information from clinical studies.

• This combined information will not be able to identify you or any other patient. This combined information may be shared with:

  • regulatory agencies,
  • doctors at other institutions,
  • the committee overseeing the ZYPREXA RELPREVY Patient Care Program, and/or
  • publications or as part of scientific discussions.

Also, by signing this form you agree to the following:

• I understand that I must enroll in the ZYPREXA RELPREVY Patient Care Program registry to get ZYPREXA RELPREVY.

• I agree to have my information entered in the ZYPREXA RELPREVY Patient Care Program registry.

• My doctor has explained the risks and benefits of treatment with ZYPREXA RELPREVY.

• I have received a copy of the Medication Guide.

• I understand that I will be observed at the clinic for 3 hours after each injection.

• Someone must go with me to my destination when I leave the clinic.

• I understand that I can not drive or use heavy machinery for the rest of the day on which I get an injection.

• I agree to seek medical care right away if I have a reaction such as excessive sleepiness, dizziness, confusion, difficulty talking, difficulty walking, muscle stiffness or shaking, weakness, irritability, aggression, anxiety, increase in blood pressure or convulsions.

• I agree to contact my doctor if I have a reaction to ZYPREXA RELPREVY.

• I may be asked to complete occasional surveys about my understanding of the risks and benefits of treatment with ZYPREXA RELPREVY.

• I or my caregiver have discussed any questions or concerns about my treatment with ZYPREXA RELPREVY with my doctor.

You may stop participating in the ZYPREXA RELPREVY Patient Care Program at any time by telling your doctor. If you stop participating, you will no longer be able to receive the drug. Your doctor will no longer provide any of your information to the ZYPREXA RELPREVY Patient Care Program except to answer safety questions. The ZYPREXA RELPREVY Patient Care Program will still use information that was collected before you stopped participating. You will be provided a copy of this form.
PATIENT INFORMATION

First Name: ___________________________ MI: _____ Last Name: ___________________________

Date of Birth: ___________________________

Gender:  □ Male  □ Female

Race:  □ White  □ Black or African American  □ Native Hawaiian or Other Pacific Islander
       □ Asian  □ American Indian or Alaska Native  □ Other

Ethnicity:  □ Hispanic or Latino  □ Non-Hispanic/Non-Latino

PRESCRIBER INFORMATION

First Name: ___________________________ MI: _____ Last Name: ___________________________

License Number: ___________________________ State of Issue: ___________________________

Treatment Facility/Practice Name (where you see the patient): ___________________________

Address Line 1: ___________________________

Address Line 2: ___________________________

Will the patient be injected/monitored at your facility/practice?

□ Yes
□ No  (If No, complete next section)

INJECTING/MONITORING FACILITY INFORMATION

Facility Name (where the patient receives injections or monitoring): ___________________________

Address Line 1: ___________________________

Address Line 2: ___________________________

City: ___________________________ State: ___________ Zip: ___________________________

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PATIENT AGREEMENT

The maker of ZYPREXA RELPREVY, Eli Lilly and Company and their delegates run the ZYPREXA RELPREVY Patient Care Program. Your doctor will send your name, date of birth, and other information that directly identifies you to the ZYPREXA RELPREVY Patient Care Program. Ask your doctor if you have questions about the information that will be collected.

The ZYPREXA RELPREVY Patient Care Program will collect and use your information in the following ways:

- Your doctor will provide dose, date and time of each injection, and other medical information to the ZYPREXA RELPREVY Patient Care Program.
- Your information will be stored in the ZYPREXA RELPREVY Patient Care Program computer system.
- The information will be used to help Lilly learn more about the safety of ZYPREXA RELPREVY.
- Information from all patients in the ZYPREXA RELPREVY Patient Care Program will be reviewed and may be combined with information from clinical studies.
- This combined information will not be able to identify you or any other patient. This combined information may be shared with:
  - regulatory agencies,
  - doctors at other institutions,
  - the committee overseeing the ZYPREXA RELPREVY Patient Care Program, and/or
  - publications or as part of scientific discussions.

Also, by signing this form you agree to the following:

- I understand that I must enroll in the ZYPREXA RELPREVY Patient Care Program registry to get ZYPREXA RELPREVY.
- I agree to have my information entered in the ZYPREXA RELPREVY Patient Care Program registry.
- My doctor has explained the risks and benefits of treatment with ZYPREXA RELPREVY.
- I have received a copy of the Medication Guide.
- I understand that I will be observed at the clinic for 3 hours after each injection.
- Someone must go with me to my destination when I leave the clinic.
- I understand that I can not drive or use heavy machinery for the rest of the day on which I get an injection.
- I agree to seek medical care right away if I have a reaction such as excessive sleepiness, dizziness, confusion, difficulty talking, difficulty walking, muscle stiffness or shaking, weakness, irritability, aggression, anxiety, increase in blood pressure or convulsions.
- I agree to contact my doctor if I have a reaction to ZYPREXA RELPREVY.
- I may be asked to complete occasional surveys about my understanding of the risks and benefits of treatment with ZYPREXA RELPREVY.
- I or my caregiver have discussed any questions or concerns about my treatment with ZYPREXA RELPREVY with my doctor.

You may stop participating in the ZYPREXA RELPREVY Patient Care Program at any time by telling your doctor. If you stop participating, you will no longer be able to receive the drug. Your doctor will no longer provide any of your information to the ZYPREXA RELPREVY Patient Care Program except to answer safety questions. The ZYPREXA RELPREVY Patient Care Program will still use information that was collected before you stopped participating. You will be provided a copy of this form.

__________
Signature

__________________________
Printed Name of Patient

__________________________
Printed Name of Legal Guardian (if applicable)

☐ Check the box if the patient has not signed due to enrollment decision being made by prescriber who is authorized via a court order.

__________________________
Date of Court Order Expiration (MMDDYYYY)

☐ This patient has been shown to be tolerant of oral olanzapine.

__________________________
Signature of Prescriber

__________________________
Printed Name of Prescriber

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Version 2.0 03A  g2012

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Reference ID: 3675779
POST-INJECTION DELIRIUM/SEDATION SYNDROME (PDSS) FORM

Submit this information within 24 hours of becoming aware of a suspected PDSS event.

Patient No (PIN)

Patient Name:

First Name

Middle Initial

Last Name

Date of Birth: 

Month

Day

Year

Does the patient have a diagnosis of schizophrenia?  □ Yes  □ No

PATIENT/INJECTION INFORMATION

Date of Injection: 

Month

Day

Year

Time of ZYPREXA RELPREV™ Injection: 

24-hour clock

Convenience Kit Package

Lot #

ONSET OF FIRST PDSS SYMPTOM AFTER INJECTION (choose only one)

□ 1 - 15 minutes

□ 16 - 30 minutes

□ 31 - 45 minutes

□ 46 - 60 minutes

□ 61 - 90 minutes (1 ½ hours)

□ 91 - 120 minutes (2 hours)

□ 121 - 150 minutes (2 ½ hours)

□ 151 - 180 minutes (3 hours)

□ If greater than 3 hours please specify:

□ _______ Hours

Dose of Injection:  □ 150 mg

□ 210 mg

□ 300 mg

□ 405 mg

□ Other dose _____ mg

Was the injection given in gluteal muscle?  □ Yes  □ No

Height:

(inches) 

Weight:

(lbs.)

PDSS SIGNS AND SYMPTOMS

Please mark the signs and symptoms that the patient experienced (check all that apply).

□ Aggressiveness

□ Agitation

□ Anxiety

□ Aspiration

□ Ataxia

□ Cardiac arrhythmias

□ Cardiopulmonary arrest

□ Coma

□ Confusion

□ Convulsion/Seizure

□ Delirium

□ Disorientation

□ Dizziness

□ Dysarthria

□ Hypertension

□ Hypotension

□ Other cognitive impairment

□ Possible neuroleptic malignant syndrome

□ Reduced level of consciousness

□ Respiratory depression

□ Sedation

□ Tachycardia

□ Various extrapyramidal symptoms

□ Weakness

□ Other __________

□ Other __________

□ Other __________

□ Other __________

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PDSS

Page 1 of 3

Reference ID: 3675779
**POST-INJECTION DELIRIUM/SEDATION SYNDROME (PDSS) FORM**

**Patient No.:**

(PIN)  

**Patient Name:**

First Name  MI  Last Name  

**PDSS start date:**  

month  day  year  

**PDSS resolution date:**

month  day  year  

OR  Ongoing

If resolved, duration of PDSS:

Minutes  Hours  Days

---

**Are these PDSS symptoms related to ZYPREXA RELPREVY?**

- Yes
- No - Please Explain

---

**Describe the clinical course**

---

**Patient Outcome: (choose one)**

- Recovered
- Fatal
- Not Recovered
- Unknown
- Recovering
- Recovered with sequelae

---

**Once a PDSS event was suspected, was the patient’s monitoring initiated in a facility capable of resuscitation?**

- Yes
- No

---

**Did the patient visit the emergency room as a result of the PDSS?**

- Yes
- No

---

**Was the patient admitted to the hospital as a result of the PDSS?**

- Yes
- No

---

**Were olanzapine concentrations collected?**

- Yes
- No

---

**Did the patient receive any MEDICATIONS AS TREATMENT for the PDSS event?**

- Yes - Please record below
- No

<table>
<thead>
<tr>
<th>Treatment Medication Name</th>
<th>Dose</th>
<th>Duration of Use (in Days)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

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**FAX 1-877-772-9391**  
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Reference ID: 3675779
POST-INJECTION DELIRIUM/SEDATION SYNDROME (PDSS) FORM

Patient No.: [ ] [ ] [ ] [ ] [ ]
(P/N)

Patient Name: ________________________ ________________________ ________________________
First Name MI Last Name

Did the patient receive any NON-PHARMACEUTICAL TREATMENTS or DIAGNOSTIC TESTS associated with this event? □ Yes - Please record below  □ No

□ Assisted ventilation  □ EEG  □ MRI  □ Urine drug screen
□ Brain CT  □ IV fluids  □ Observation/symptomatic management  □ Vital sign monitoring
□ ECG  □ Labs  □ Restraints  □ Other ____________________________

Please fax test results to 1-877-772-9391.

HISTORY PRIOR TO PDSS EVENT

Does the patient have any relevant comorbidities?

□ Yes - Please specify: __________________________________________
□ No

PRIOR MEDICATIONS

Did the patient take any medications during the 24 hours prior to the injection? □ Yes - Please record below  □ No

<table>
<thead>
<tr>
<th>Prior Medication Name</th>
<th>Dose</th>
<th>Duration of Use</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Number</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Days</td>
</tr>
</tbody>
</table>

Did the patient use any of the following during the 24 hours prior to the injection? □ Yes - Please record below  □ No

□ Alcohol  □ Barbiturates  □ Cocaine  □ Opiates
□ Amphetamines/Methamphetamines  □ Cannabinoid  □ Hallucinogens  □ Phencyclidine

Event reported by: ________________________ ________________________ ________________________
First MI Last

Title/Occupation: ________________________ ________________________ ________________________

If agent of the Prescriber, name of Prescriber: ________________________ ________________________ ________________________

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Reference ID: 3675779
PHARMACY REGISTRATION FORM

To be enrolled in the ZYPREXA RELPREVV Patient Care Program, complete and fax this form to 1-877-772-9391.

Training must be completed before a pharmacy may be enrolled in the ZYPREXA RELPREVV Patient Care Program.

PHARMACY INFORMATION

☐ Enrollment  ☐ Reenrollment
Pharmacy/Hospital Name: ________________________________
Pharmacy DEA Number: ________________________________
Please specify description of Pharmacy: ☐ Community/Retail  ☐ Specialty Pharmacy  ☐ Hospital or Institution  ☐ Other
Address Line 1: __________________________________________
Address Line 2: __________________________________________
City: ______________________  State: ______________  Zip: __________
Primary Phone: ______________________  Secondary Phone: __________
Fax: ____________________________

SHIP TO INFORMATION

Ship To Address (if the same as above, check here)  ☐
Ship To Contact Name: ________________________________
Address Line 1: __________________________________________
Address Line 2: __________________________________________
City: ______________________  State: ______________  Zip: __________
Primary Phone: ______________________  Secondary Phone: __________
Fax: ____________________________

PHARMACIST-IN-CHARGE INFORMATION

First Name: ____________________  MI: ______  Last Name: ____________________
Email: __________________________
Phone: __________________________  Fax: __________________________
(if different from above)  (if different from above)

PHARMACIST-IN-CHARGE INFORMATION

By signing below, I acknowledge that:

- I have read and understand the ZYPREXA RELPREVV Patient Care Program Instructions Brochure.
- I will ensure that all appropriate pharmacy staff are trained and have read and understand the ZYPREXA RELPREVV Patient Care Program Instructions Brochure.
- I will ensure that all appropriate pharmacy staff understand that ZYPREXA RELPREVV can only be dispensed for use in certain health care settings (e.g., hospitals, clinics) that have ready access to emergency response services and that can allow for continuous patient monitoring for at least 3 hours post-injection.
- I will ensure that pharmacy staff will verify that the patient is enrolled in the ZYPREXA RELPREVV Patient Care Program registry prior to dispensing each prescription/refill by accessing the system.
- I will ensure that pharmacy staff will not dispense ZYPREXA RELPREVV directly to patients.
- I will ensure pharmacy staff report the date of each ZYPREXA RELPREVV dispensing to the ZYPREXA RELPREVV Patient Care Program.
- For each dispense I will ensure prescription verification (includes patient eligibility check and recording the dispense date) is completed on the date of dispensing, prior to the convenience kit leaving the pharmacy.
- I understand that the ZYPREXA RELPREVV Patient Care Program Coordinating Center may contact the pharmacy to clarify information provided or obtain information about the patient.

I may cancel this registration by notifying the ZYPREXA RELPREVV Patient Care Program Coordinating Center by fax at 1-877-772-9391 or by phone at 1-877-772-9390. If I cancel, Lilly will cease to supply ZYPREXA RELPREVV to the pharmacy.

Pharmacist-in-Charge Signature __________________________________________

Date: ____________   month - ____________   day - ____________   year ______

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Version 4.0 08Sept2014

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Reference ID: 3675779
To be enrolled in the ZYPREXA RELPREVX Patient Care Program, complete and fax this form to 1-877-772-9391.

Training must be completed before a prescriber may be enrolled in the ZYPREXA RELPREVX Patient Care Program.

**PRESCRIBER INFORMATION**

- [ ] Enrollment
- [ ] Reenrollment

First Name: ___________________________________________ MI: ______ Last Name: ___________________________________________

Degree: [ ] MD [ ] DO [ ] NP [ ] PA [ ] Nurse with prescriptive authority [ ] Other with prescriptive authority

License Number: __________________________ State of Issue: __________________________

Treatment Facility/Practice (Where you see your patients): __________________________________________

If you see your patients at multiple locations please contact the ZYPREXA RELPREVX Patient Care Program Coordinating Center to provide additional facility/practice information

Address Line 1: __________________________________________

Address Line 2: __________________________________________

City: __________________________ State: __________ Zip: __________________________

Phone: __________________________ Alternate Phone: __________________________

Fax: __________________________ Prescriber Email: __________________________

Preferred Method of Communication: [ ] Email [ ] Fax

**PRESCRIBER AGREEMENT**

By signing below, I acknowledge that:

- I understand the ZYPREXA RELPREVX Patient Care Program requirements and the risks associated with ZYPREXA RELPREVX.
- I have completed the mandatory ZYPREXA RELPREVX training.
- I understand the clinical presentation of post-injection delirium/sedation syndrome (PDSS) and how to manage patients should an event occur while using ZYPREXA RELPREVX.
- I understand that ZYPREXA RELPREVX should only be initiated in patients for whom tolerability with oral olanzapine has been established.
- I understand that ZYPREXA RELPREVX should only be administered to patients in healthcare settings (e.g., hospitals, clinics) that have ready access to emergency response services and that can allow for continuous patient monitoring for at least 3 hours post-injection.
- I will enroll all patients in the ZYPREXA RELPREVX Patient Care Program registry prior to prescribing ZYPREXA RELPREVX by completing the Patient Registration Form.
- I will ensure all suspected cases of PDSS are reported to the ZYPREXA RELPREVX Patient Care Program within 24 hours of becoming aware of the event.
- I will review the ZYPREXA RELPREVX Medication Guide with each patient prior to prescribing.
- I understand that the ZYPREXA RELPREVX Patient Care Program Coordinating Center may contact me to resolve discrepancies, to obtain information about a patient, or to conduct occasional surveys.

I may cancel this registration by notifying the ZYPREXA RELPREVX Patient Care Program Coordinating Center by fax at 1-877-772-9391 or by phone at 1-877-772-9390.

If I revoke my registration, I will no longer be eligible to prescribe ZYPREXA RELPREVX.

Lilly may disenroll prescribers that are non-compliant with the program requirements.

________________________________________
Prescriber Signature

______________________
Date: ____________ - ____________ - ____________

**PHONE 1-877-772-9390**

**FAX 1-877-772-9391**

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Version 2.0 03Aug2012

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Lilly

Reference ID: 3675779
SINGLE PATIENT INJECTION FORM

ZYPREXA® RELPREVV® (olanzapine) For Extended Release Injectable Suspension

IMPORTANT: Before administering the injection, confirm there will be someone to accompany the patient after the 3-hour observation period. If this cannot be confirmed, do not give the injection.

Submit this information within 7 days after the patient’s injections. If you are aware that the patient’s prescriber has changed, please notify the ZYPREXA RELPREVV Patient Care Program Coordinating Center.

Patient No.: [ ] [ ] [ ] [ ] [ ] [ ]
PIN: [ ] [ ] [ ] [ ] [ ]
Injection Facility Name: ____________________________
Patient Name: ____________________________
First: ____________________________ MI: ____________________________ Last: ____________________________
Date of Birth: [ ] [ ] [ ] [ ] [ ] [ ]
month day year

PDSS since the last visit? (After the patient left the office, following his/her previous injection, did the patient experience post-injection delirium/sedation syndrome?)
☐ No ☐ Yes
If Yes, has the prescriber been notified of the PDSS event?
☐ Yes ☐ No

ZYPREXA RELPREVV TREATMENT

Date of Injection: [ ] [ ] [ ] [ ] [ ] [ ]
month day year

Time of ZYPREXA RELPREVV injection: [ ] [ ]
24-hour clock

Dose of Injection: ☐ 150 mg ☐ 210 mg ☐ 300 mg ☐ 405 mg ☐ Other dose _________ mg

Was the patient observed for at least 3 hours post-injection? ☐ Yes ☐ No

Did the patient experience post-injection delirium/sedation syndrome during the onsite post-injection observational period?
☐ No ☐ Yes
If Yes, has the prescriber been notified of the PDSS event? ☐ Yes ☐ No

Following the injection, was the patient alert, oriented, and absent of any signs and symptoms of PDSS prior to being released from the healthcare facility?
☐ Yes ☐ No

Following the injection, was the patient accompanied from the facility?
☐ Yes ☐ No ☐ Not applicable, patient did not leave facility (in-patient)

Was the patient or legal guardian given a Medication Guide prior to this injection? ☐ Yes ☐ No

__________________________ ____________________________
Healthcare Facility Staff Member Signature DATE: [ ] [ ] [ ]
month day year

Healthcare Facility Staff Member Name (print): ____________________________

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Reference ID: 3675779
HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use ZYPREXA RELPREV™ safely and effectively. See full prescribing information for ZYPREXA RELPREV. ZYPREXA RELPREV (olanzapine) For Extended Release Injectable Suspension

Revised: 07/2011

WARNING: POST-INJECTION DELIRIUM/SEDATION SYNDROME AND INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

See full prescribing information for complete boxed warning.

- Patients are at risk for severe sedation (including coma) and/or delirium after each injection and must be observed for at least 3 hours in a registered facility with ready access to emergency response services. Because of this risk, ZYPREXA RELPREV is available only through a restricted distribution program called ZYPREXA RELPREV Patient Care Program and requires prescriber, healthcare facility, patient, and pharmacy enrollment. (2.1, 5.1, 5.2, 10.2, 17.3)
- Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. ZYPREXA RELPREV is not approved for the treatment of patients with dementia-related psychosis. (5.3, 5.5, 17.3)

- Neutropenic Malignant Syndrome: Manage with immediate discontinuation and close monitoring. (5.5)
- Hyperpyrexia: In some cases extremely elevated body temperature with or without mental status changes. (5.6)
- Hypertension: Observe for significant increases in blood pressure. (5.6.1)
- Hypoventilation: Unintentional weight loss of 10% of body weight over 6 months. (5.6.3)
- Cardiac arrhythmia: Observe for tachycardia and/or sinus tachycardia. (5.6.4)
- Orthostatic Hypotension: Orthostatic hypotension associated with dizziness, lightheadedness, or syncope. (5.10)

RECENT MAJOR CHANGES

INDICATIONS AND USAGE

ZYPREXA® RELPREV™ is a long-acting injectable antipsychotic for intramuscular administration indicated for the treatment of schizophrenia. (1.1)

Efficacy was established in two clinical trials in patients with schizophrenia: one 8-week trial in adults and one maintenance trial in adults. (14.1)

DOSAGE AND ADMINISTRATION

150 mg/2 ml, 300 mg/4 ml, 210 mg/2 ml, 405 mg/4 ml, or 300 mg/2 ml. See Table 1 for dosing recommendations. (2.1)

ZYPREXA RELPREV is intended for deep intramuscular gluteal injection only.

- Do not administer intravenously or subcutaneously. (2.2)
- Average: 405 mg or 300 mg every 4 weeks. (2.2)
- Use in specific populations (including renal and hepatic impaired, and pediatric population) has not been studied. (2.2)
- Must be suspended using only the diluent for ZYPREXA RELPREV provided in the convenience kit. (2.2)

DOSAGE FORMS AND STRENGTHS

Powder for suspension for intramuscular use only: 210 mg/ml, 300 mg/ml, and 405 mg/ml (2.1, 11.18)

CONTRAINDICATIONS

Note:

- Elderly Patients with Dementia-Related Psychosis: Increased risk of death and increased incidence of cerebrovascular adverse events (e.g., stroke, transient ischemic attack). (5.3)
- Suicide: The possibility of a suicide attempt is inherent in schizophrenia, and close supervision of high-risk patients who are likely to attempt suicide may be necessary. (5.3)

FULL PRESCRIBING INFORMATION:

CONTENTS

WARNING: POST-INJECTION DELIRIUM/SEDATION SYNDROME AND INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

1 INDICATIONS AND USAGE
1.1 Schizophrenia

2 DOSAGE AND ADMINISTRATION
2.1 Dosage
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REFERENCES:

- Sections or subsections omitted from the full prescribing information are not listed.

ZYPREXA RELPREV (olanzapine)
For Extended Release Injectable Suspension

PV 5924 AMP

ZYPREXA RELPREV (olanzapine)
For Extended Release Injectable Suspension

PV 5924 AMP
If post-injection delirium/sedation syndrome is suspected, close medical supervision and monitoring should be instituted in a facility capable of resuscitation (see Overdosage (10)).

Dosing in Specific Populations — Tolerance of oral ZYPREXA may not be established prior to initiating treatment with ZYPREXA RELPREVV. The recommended starting dose is ZYPREXA RELPREVV 150 mg/4 wks in patients who are debilitated, who have a predisposition to hypotensive reactions, who otherwise exhibit a combination of factors that may result in slower metabolism of olanzapine (e.g., nonsmoking female patients ≥65 years of age), or who may be more pharmacodynamically sensitive to olanzapine. When indicated, dose escalation should be undertaken with caution in these patients (see Warnings and Precautions (5.4, Drug Interactions (7), and Clinical Pharmacology (12.3)).

ZYPREXA RELPREVV has not been studied in subjects under 18 years of age (see Warnings and Precautions (5.6, 5.7, and 5.8)).

Maintenance Treatment — Although no controlled studies have been conducted to determine how long patients should be treated with ZYPREXA RELPREVV, efficacy has been demonstrated over a period of 24 weeks in patients with stabilized schizophrenia. Additionally, oral ZYPREXA has been shown to be effective in maintenance treatment response in schizophrenia in longer-term use. Patients should be periodically reassessed to determine the need for continued treatment.

Switching from Other Antipsychotics — There are no systematically collected data to specifically address how to switch patients with schizophrenia from other antipsychotics to ZYPREXA RELPREVV.

2.2 Instructions to Reconstitute and Administer ZYPREXA RELPREVV

For deep intramuscular gluteal injection only. Not to be injected intravenously or subcutaneously.

Step 1: Preparing Materials

Convenience kit includes:

- Vial of ZYPREXA RELPREVV powder
- • 3-mL vial of diluent
- • 1 mL of diluent with pre-attached 19-gauge, 1.5-inch (38 mm) Hypodermic Needle-Pro® needle with needle protection device
- • Two 19-gauge, 1.5-inch (38 mm) Hypodermic Needle-Pro needles with needle protection device

For obese patients, a 2-inch (5 cm), 19-gauge or larger needle (not included in convenience kit) may be used for administration.

ZYPREXA RELPREVV must be suspended using only the diluent supplied in the convenience kit.

It is recommended that gloves are used when reconstituting, as ZYPREXA RELPREVV may be irritating to the skin. Flush with water if contact is made with skin.

See additional insert entitled “Instructions to Reconstitute and Administer ZYPREXA RELPREVV” (included) for more information regarding the safe and effective use of the Hypodermic Needle-Pro syringe and needle.

Step 2: Determining Reconstitution Volume

Refer to the table below to determine the amount of diluent to be added for reconstitution of each vial strength.

It is important to note that there is more diluent in the vial than is needed to reconstitute.

<table>
<thead>
<tr>
<th>Vial Strength</th>
<th>Diluent to Add</th>
</tr>
</thead>
<tbody>
<tr>
<td>150 mg</td>
<td>1.5 mL</td>
</tr>
<tr>
<td>210 mg</td>
<td>1 mL</td>
</tr>
<tr>
<td>300 mg</td>
<td>1.6 mL</td>
</tr>
<tr>
<td>405 mg</td>
<td>2.3 mL</td>
</tr>
</tbody>
</table>

Step 3: Reconstituting ZYPREXA RELPREVV

Please read the Hypodermic Needle-Pro Instructions for Use before proceeding with Step 3. Failure to follow these instructions may result in a needless injury.

Loosen the powder by lightly tapping the vial.

Open the prepackaged Hypodermic Needle-Pro syringe and needle with needle protection device. Withdraw the pre-determined diluent volume (Step 2) into the syringe.

Inject the diluent into the powder vial.

Withdraw air to equalize the pressure in the vial by pulling back slightly on the plunger in the syringe.

Remove the needle from the vial, holding the vial upright to prevent any loss of material. Engage the needle safety device (refer to complete Hypodermic Needle-Pro Instructions for Use).

Pad a hard surface to cushion impact (see Figure 1). Tap the vial firmly and repeatedly on the surface until no powder is visible.

ZYPREXA RELPREVV has not been studied in subjects under 18 years of age (see Warnings and Precautions (5.6, 5.7, and 5.8)).

Additional tapping may be required if large clumps remain (see Figure 2).
related psychosis [see Boxed Warning, Warnings and Precautions (5.16), and Patient Counseling Information (7.3)].

In placebo-controlled oral olanzapine clinical trials of elderly patients with dementia-related psychosis, the incidence of death in olanzapine-treated patients was significantly greater than placebo-treated patients (3.5% vs 1.5%, respectively).

Cerebrovascular Adverse Events (OASIS), Including Stroke

Cerebrovascular adverse events (e.g., stroke, transient ischemic attacks) included fatal events, were reported in patients in trials of oral olanzapine in elderly patients with dementia-related psychosis. In placebo-controlled trials, there was a significantly higher incidence of cerebrovascular adverse events in patients treated with oral olanzapine compared to patients treated with placebo. ZIPREXELA was not approved for the treatment of patients with dementia-related psychosis [see Boxed Warning and Patient Counseling Information (7.3)].

5.4 Suicide

The possibility of a suicide attempt is inherent in schizophrenia, and close supervision of high-risk patients should accompany drug therapy.

5.5 Neuropsychiatric Malignant Syndrome (NMS)

A potentially fatal complex symptom syndrome sometimes referred to as Neuropsychiatric Malignant Syndrome (NMS) has been reported in association with administration of antipsychotic drugs, including olanzapine. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability with2 a mean or marked tachycardia, blood pressure fluctuation, hyperpyrexia, diaphoresis and cardia dysrhythmia. Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure.

The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to exclude cases where the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and unattributed or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever, and primary central nervous system pathology.

The management of NMS should include: 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy; 2) intensive symptomatic treatment and medical monitoring; and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no generally agreed upon specific pharmacological treatment regimen for NMS.

If a patient requires antipsychotic drug therapy after recovery from NMS, the potential reintroduction of drug therapy should be considered carefully and tolerance with oral olanzapine should be established prior to initiating treatment with ZIPREXELA [see Dosage and Administration (2.1)]. The patient should be carefully monitored, since remissions of NMS have been reported [see Patient Counseling Information (7.4)].

5.6 Hyperglycemia

Physicians should consider the risks and benefits when prescribing olanzapine to patients with an established diagnosis of diabetes mellitus, or to those with undiagnosed increased fasting glucose level (fasting 100–126 mg/dL, nonfasting 140–200 mg/dL). Patients taking olanzapine should be monitored regularly for worsening of glucose control. Patients starting treatment with olanzapine should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with antipsychotic agents should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with antipsychotic agents should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug [see Patient Counseling Information (7.5)].

Hyperglycemia, in some cases extreme and associated with ketoadsorption or hyperosmolar coma or death, has been reported in patients treated with antipsychotic agents including olanzapine. Assessment of the relationship between antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Epidemiologic studies suggest an increased risk of treatment-emergent hyperglycemia-related adverse reactions in patients treated with the antipsychotics. While relative risk estimates are inconsistent, the association between antipsychotic use and increases in glucose levels appears to fall on a continuum and olanzapine appears to have a greater association than other antipsychotic drugs.

Mean increases in blood glucose have been observed in patients treated in median exposure of 0.2 months (with observation time of 1 of the Clinical Trials of Olanzapine Monotherapy). The mean increase of serum glucose (fasting and nonfasting samples) from baseline to the average of the 2 highest serum concentrations was 15.0 mg/dL.

In a study of healthy volunteers, subjects who received olanzapine (N=22) for 3 weeks had a mean increase in fasting blood glucose of 2.2 mg/dL. Placebo-treated subjects (N=10) had a mean increase in fasting blood glucose compared to baseline of 0.34 mg/dL.

Olanzapine Monotherapy: Adults—In an analysis of 5 placebo-controlled adult olanzapine monotherapy studies in schizophrenia (range of dosages 10–20 mg/day), olanzapine was associated with a greater mean change in fasting glucose levels compared to placebo (2.75 mg/dL versus 0.17 mg/dL). The difference in mean change between olanzapine and placebo was greater in patients with evidence of glucose dysregulation at baseline (patients diagnosed with diabetes mellitus or related adrenergic reactions, patients treated with antidiabetic agents, patients with a baseline random glucose level ≥200 mg/dL, and/or baseline fasting glucose level ≥125 mg/dL).

Table 2: Changes in Fasting Glucose Levels from Adult Olanzapine Monotherapy Studies

<table>
<thead>
<tr>
<th>Laboratory Analyte</th>
<th>Category Change (at least once) from Baseline</th>
<th>Treatment Arm</th>
<th>Patients</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Glucose</td>
<td>Normal to High (&gt;100 mg/dL, to ≤126 mg/dL)</td>
<td>Olanzapine</td>
<td>43.2%</td>
<td>34.9%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo</td>
<td>38.6%</td>
<td>39.4%</td>
</tr>
<tr>
<td></td>
<td>Serendipity to High (≥100 mg/dL, and ≤126 mg/dL)</td>
<td>Olanzapine</td>
<td>17.6%</td>
<td>17.4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo</td>
<td>17.0%</td>
<td>17.6%</td>
</tr>
<tr>
<td>Non-fasting Glucose</td>
<td>Normal to High (&gt;100 mg/dL, to ≤126 mg/dL)</td>
<td>Olanzapine</td>
<td>91.8%</td>
<td>91.6%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo</td>
<td>91.0%</td>
<td>90.7%</td>
</tr>
</tbody>
</table>

* Not Applicable.

The mean change in fasting glucose for patients exposed at least 48 weeks was 4.2 mg/dL (N=487). In analyses of olanzapine in completed 6–12 months of olanzapine therapy, mean changes in fasting and nonfasting glucose levels continued to increase over time.
Olanzapine Monotherapy in Adolescents — The safety and efficacy of ZYPREXA RELPREVV have not been established in patients under the age of 18 years. In an analysis of 3 placebo-controlled oral olanzapine monotherapy studies of adolescent patients (13-17 years), including those with schizophrenia (6 weeks) or bipolar I disorder (manic or mixed episodes) (3 weeks), olanzapine was associated with a greater mean change from baseline in fasting glucose levels compared to placebo (2.68 mg/dL versus -2.59 mg/dL). The mean change in fasting glucose for adolescents exposed at least 24 weeks was 3.1 mg/dL (N=121). Table 3 shows short-term and long-term changes in fasting blood glucose from adolescent oral olanzapine monotherapy studies.

Table 3: Changes in Fasting Glucose Levels from Adolescent Oral Olanzapine Monotherapy Studies

<table>
<thead>
<tr>
<th>Laboratory Analyte</th>
<th>Category Change (at least once) from Baseline</th>
<th>Treatment Arm</th>
<th>Up to 12 weeks exposure</th>
<th>At Least 24 weeks exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Glucose</td>
<td>Normal to High (&lt;100 mg/dL to &gt;126 mg/dL)</td>
<td>Olanzapine 124</td>
<td>9%</td>
<td>108</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo 53</td>
<td>1.9%</td>
<td>NA</td>
</tr>
<tr>
<td>Borderline to High (100 mg/dL and &lt;126 mg/dL to &gt;126 mg/dL)</td>
<td>Olanzapine 14</td>
<td>14.3%</td>
<td>13.2%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo 13</td>
<td>0%</td>
<td>NA</td>
</tr>
</tbody>
</table>

* Not Applicable.

In long-term studies (at least 24 weeks), adolescents had increases from baseline in mean fasting total cholesterol, LDL cholesterol, and triglycerides of 5.5 mg/dL, 5.4 mg/dL, and 20.5 mg/dL, respectively, and a mean decrease in fasting HDL cholesterol of 4.5 mg/dL. Table 5 shows categorical changes in fasting lipids values in adolescents.

Table 5: Changes in Fasting Lipids Values from Adolescent Oral Olanzapine Monotherapy Studies

<table>
<thead>
<tr>
<th>Laboratory Analyte</th>
<th>Category Change (at least once) from Baseline</th>
<th>Treatment Arm</th>
<th>Up to 6 weeks exposure</th>
<th>At Least 24 weeks exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Triglycerides</td>
<td>Increase by ≥50 mg/dL to ≤200 mg/dL</td>
<td>Olanzapine 136</td>
<td>37.0%</td>
<td>122</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo 56</td>
<td>15.2%</td>
<td>NA</td>
</tr>
<tr>
<td>Borderline to High (&lt;90 mg/dL to &gt;130 mg/dL)</td>
<td>Olanzapine 87</td>
<td>29.3%</td>
<td>66.3%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo 29</td>
<td>10.7%</td>
<td>NA</td>
</tr>
<tr>
<td>Borderline to High (&gt;90 mg/dL and ≤130 mg/dL to &gt;130 mg/dL)</td>
<td>Olanzapine 37</td>
<td>59.5%</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo 17</td>
<td>35.3%</td>
<td>NA</td>
</tr>
<tr>
<td>Increase by ≥40 mg/dL</td>
<td>Olanzapine 124</td>
<td>14.5%</td>
<td>122</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo 60</td>
<td>4.5%</td>
<td>NA</td>
</tr>
</tbody>
</table>

* Not Applicable.

| Fasting Total Cholesterol | Normal to High (>170 mg/dL and ≤200 mg/dL) | Olanzapine 87 | 6.9%                     | 78                        |
|                          |                                              | Placebo 43    | 2.3%                     | NA                        |
| Borderline to High (>170 mg/dL and <130 mg/dL to >130 mg/dL) | Olanzapine 36 | 30.9%                    | 33                        |
|                          |                                              | Placebo 13    | 7.7%                     | NA                        |

In long-term studies (at least 24 weeks), mean fasting total cholesterol, LDL cholesterol, and triglycerides of 1.3 mg/dL, 1.0 mg/dL, and a decrease in triglycerides of 11.1 mg/dL for placebo-treated adolescents. For fasting HDL cholesterol, no clinically meaningful differences were observed between olanzapine-treated adolescents and placebo-treated adolescents.

Table 4: Changes in Fasting Lipids Values from Adult Olanzapine Monotherapy Studies

<table>
<thead>
<tr>
<th>Laboratory Analyte</th>
<th>Category Change (at least once) from Baseline</th>
<th>Treatment Arm</th>
<th>Up to 12 weeks exposure</th>
<th>At Least 24 weeks exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Triglycerides</td>
<td>Increase by ≥50 mg/dL</td>
<td>Olanzapine 143</td>
<td>17.5%</td>
<td>121</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo 63</td>
<td>11.1%</td>
<td>NA</td>
</tr>
<tr>
<td>Borderline to High (&lt;100 mg/dL to ≥130 mg/dL)</td>
<td>Olanzapine 98</td>
<td>5.1%</td>
<td>92</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo 46</td>
<td>4.5%</td>
<td>NA</td>
</tr>
<tr>
<td>Borderline to High (&gt;110 mg/dL and ≤130 mg/dL to &gt;130 mg/dL)</td>
<td>Olanzapine 29</td>
<td>48.3%</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo 9</td>
<td>0%</td>
<td>NA</td>
</tr>
</tbody>
</table>

* Not Applicable.

In long-term studies (at least 24 weeks), the mean weight gain was 11.2 kg (24.6 lb); (median exposure to 6 weeks). 22.2% of olanzapine-treated patients gained at least 7% of their baseline weight, compared to 3% of placebo-treated patients, with a median exposure to event of 8 weeks; 4.2% of olanzapine-treated patients gained at least 15% of their baseline weight, compared to 0.3% of placebo-treated patients, with a median exposure to event of 12 weeks. Clinically significant weight gain was observed across all baseline Body Mass Index (BMI) categories. Discontinuation due to weight gain occurred in 0.2% of olanzapine-treated patients and in 0% of placebo-treated patients.

In long-term studies (at least 48 weeks), the mean weight gain was 5.6 kg (12.3 lb) (median observation of 573 days, N=201). The percentages of patients who gained at least 15%, 25%, or 75% of their baseline body weight with long-term exposure were 15.4%, 32.1%, and 12.0%, respectively. Discontinuation due to weight gain occurred in 0.4% of olanzapine-treated patients following at least 48 weeks of exposure.

Table 6 includes data on adult weight gain with olanzapine pooled from 86 clinical trials. The data in each column represent data for those patients who completed treatment periods of the durations specified.

Table 7: Weight Gain with Oral Olanzapine Use in Adolescents from 4 Placebo-Controlled Trials

<table>
<thead>
<tr>
<th>Amount Gained (lb)</th>
<th>6 Weeks (N=7465) (%)</th>
<th>6 Months (N=1462) (%)</th>
<th>12 Months (N=1345) (%)</th>
<th>24 Months (N=474) (%)</th>
<th>36 Months (N=147) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>26.2</td>
<td>24.3</td>
<td>20.8</td>
<td>23.2</td>
<td>17.0</td>
</tr>
<tr>
<td>0 to ≤5 (0-11 lb)</td>
<td>57.0</td>
<td>39.0</td>
<td>26.0</td>
<td>23.4</td>
<td>25.2</td>
</tr>
<tr>
<td>&gt;5 to ≤11 (12-22 lb)</td>
<td>17.4</td>
<td>24.6</td>
<td>24.2</td>
<td>24.1</td>
<td>18.4</td>
</tr>
<tr>
<td>&gt;11 to ≤15 (23-33 lb)</td>
<td>10.0</td>
<td>14.9</td>
<td>11.4</td>
<td>11.7</td>
<td>17.0</td>
</tr>
<tr>
<td>&gt;15 to ≤20 (34-44 lb)</td>
<td>9.1</td>
<td>3.1</td>
<td>8.6</td>
<td>9.3</td>
<td>11.6</td>
</tr>
<tr>
<td>&gt;20 to ≤25 (45-55 lb)</td>
<td>0.7</td>
<td>0.3</td>
<td>3.3</td>
<td>5.1</td>
<td>4.1</td>
</tr>
<tr>
<td>&gt;25 to ≤30 (56-66 lb)</td>
<td>0.1</td>
<td>0.2</td>
<td>1.4</td>
<td>2.3</td>
<td>4.8</td>
</tr>
<tr>
<td>&gt;30 (&gt;66 lb)</td>
<td>0.0</td>
<td>0.0</td>
<td>0.8</td>
<td>1.2</td>
<td>2.0</td>
</tr>
</tbody>
</table>

In long-term studies (at least 24 weeks), the mean weight gain was 11.2 kg (24.6 lb); (median exposure of 201 days, N=179). The percentages of adolescents who gained at least 7%, 15%, or 25% of their baseline body weight with long-term exposure were 89%, 55%, and 29%, respectively. Among adolescent patients, mean weight gain by BMI category was 11.5 kg (25.3 lb); 12.1 kg (26.8 lb), and 12.5 kg (27.6 lb), respectively.
12.7 kg (27.9 lb), respectively, for normal (N=106), overweight (N=28) and obese (N=17). Discontinuation due to weight gain occurred in 2.2% of olanzapine-treated patients following at least 24 weeks of exposure.

Table 8 shows data on adolescent weight gain with olanzapine pooled from 6 clinical trials. The data in each column represent data for those patients who completed treatment periods of the durations specified. Little clinical trial data is available on weight gain in adolescents with olanzapine beyond 6 months of treatment.

Table 8: Weight Gain with Olanzapine Use in Adolescents

| Amount Gained (kg) | 0-0 | 0.5-0 | 0-1 | 1-2 | 1-3 | 2-3 | ≥3 | 4-5 | 4-6 | 5-6 | 6-7 | 7-8 | 8-9 | 9-10 | 10-11 | 11-12 | 12-13 | 13-14 | 14-15 | 15-16 | 16-17 | 17-18 | 18-19 | ≥19
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>6 Weeks (N=243)</td>
<td></td>
<td></td>
<td>1.3</td>
<td>1.8</td>
<td>2.7</td>
<td>2.7</td>
<td>3</td>
<td>3.5</td>
<td>4.2</td>
<td>4.2</td>
<td>4.2</td>
<td>4.8</td>
<td>5.1</td>
<td>5.4</td>
<td>6.2</td>
<td>6.7</td>
<td>7.1</td>
<td>7.6</td>
<td>8.2</td>
<td>8.7</td>
<td>9.2</td>
<td>10.0</td>
<td>10.7</td>
<td></td>
</tr>
<tr>
<td>6 Months (N=191)</td>
<td>2.9</td>
<td>4.0</td>
<td>4.7</td>
<td>6.2</td>
<td>8.3</td>
<td>9.2</td>
<td>10.4</td>
<td>11.6</td>
<td>12.5</td>
<td>13.7</td>
<td>14.7</td>
<td>16</td>
<td>17.1</td>
<td>18.6</td>
<td>20.6</td>
<td>22.8</td>
<td>24.9</td>
<td>27.1</td>
<td>29.3</td>
<td>31.5</td>
<td>33.7</td>
<td>35.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5.9 Tardive Dyskinesia

A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially women, this syndrome is not likely to rely upon exposure estimates to predict, at the inception of antipsychotic treatment, which patients are likely to develop the syndrome. Whether antipsychotic drug products differ in their potential to cause tardive dyskinesia is unknown.

The risk of developing tardive dyskinesia and the likelihood that it will become irreversible are believed to increase with the duration of treatment and the total cumulative dose of antipsychotic drugs tolerated by the patient. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses or may even arise after discontinuation of treatment. There is no demonstrable relationship between late age or long duration of illness and tardive dyskinesia, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. Antiparkinsonian treatment, itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown.

Given these considerations, olanzapine should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Patients whose movement disorder should generally be reserved for patients (1) who suffer from a chronic illness that is known to respond to antipsychotic drugs, and (2) for whom alternative, equally effective, but potentially less harmful treatments are not available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically.

If signs and symptoms of tardive dyskinesia appear in a patient on olanzapine, drug discontinuation should be considered. However, some patients may require treatment with olanzapine despite the presence of the syndrome.

5.10 Orthostatic Hypotension

ZYPREXA RELPREVV may induce orthostatic hypotension associated with dizziness, tachycardia, bradycardia, and/or syncope. In some patients, syncope, probably reflecting its α1-adrenergic antagonistic properties [see Patient Counseling Information (17.8)], has been reported. Patients who are volume-depleted, e.g., elderly hypertensive patients, or have conditions which predispose patients to hypotension (dehydration, hypovolemia, and treatment with antihypertensive medications) when the occurrence of syncope, hypotension and/or bradycardia might put the patient at increased medical risk. For patients in this population who have never taken a drug with antihypertensive properties, it should be established with oral olanzapine prior to initiating treatment with ZYPREXA RELPREVV [see Dosage and Administration (2.1)].

Caution is necessary in patients who receive treatment with other drugs having effects that can induce syncope, or hypotension and/or bradycardia might put the patient at increased medical risk. For patients in this population who have never taken a drug with antihypertensive properties, it should be established with oral olanzapine prior to initiating treatment with ZYPREXA RELPREVV [see Dosage and Administration (2.1)].

5.11 Leukopenia, Neutropenia, and Agranulocytosis

Leukopenia, neutropenia, and agranulocytosis were reported temporally related to antipsychotic agents, including ZYPREXA. Agranulocytosis has also been reported.

Possible risk factors for leukopenia/neutropenia include pre-existing low white blood cell count (WBC) and history of drug-induced leukopenia/neutropenia. Patients with a history of a clinically significant low WBC or drug induced leukopenia/neutropenia should have their complete blood count monitored frequently during the study. Olanzapine is not approved for the treatment of patients with leukemia.

5.12 Dysphagia

Dysphagia

Esophageal dysmotility and aspiration have been associated with antipsychotic drug use. Aspiration pneumonia is a potential cause of morbidity and mortality in patients with advanced Alzheimer’s disease. Olanzapine is not approved for the treatment of patients with Alzheimer’s disease.

5.13 Seizures

Premature treatment discontinuation of ZYPREXA RELPREVV, seizures occurred in 0.15% of patients. During premature treatment discontinuation of ZYPREXA RELPREVV, seizures occurred in 0.1% of olanzapine-treated patients. There were no seizures reported in the placebo group. The rate of discontinuation due to seizure was within the 2% range for placebo patients (2% [3/168] of females, 2% [7/286] of males) and placebo patients (2% [49/3240] of females), sexual function-related events (2% [51/8136] of females and males), and breast-related events (0% [23/2342] of females), and breast-related events (0% [17/454] of females and males) and breast-related events (0% [3/168] of females, 2% [7/286] of males) [see Use in Specific Populations (8.4)].

5.14 Potential for Cognitive and Motor Impairment

Seizures were commonly reported adverse reaction associated with ZYPREXA RELPREVV treatment, occurring at an incidence of 8% in ZYPREXA RELPREVV patients compared to 2% in placebo patients. Somnolence and sedation adverse reactions led to discontinuation in 0.6% of patients in the premaintenance ZYPREXA RELPREVV database.

5.15 Body Temperature Regulation

The ability of the body to reduce core temperature has been attributed to antipsychotic agents.

5.16 Use in Patients with Concomitant Illness

Experience with ZYPREXA RELPREVV in patients with concomitant systemic illnesses is limited [see Clinical Pharmacology (12.3)].

5.17 Hyperprolactinemia

As with other drugs that antagonize dopamine D2 receptors, olanzapine elevates prolactin levels, and the elevation persists during chronic administration. Hyperprolactinemia may suppress hypothalamic GnRH, resulting in reduced pituitary gonadotropin secretion. This, in turn, may inhibit reproductive function by impairing gonadal function in both female and male patients. Galactorrhea, amenorrhea, gynecomastia, and impotence have been reported in patients receiving prolactin-elevating compounds. Long-acting antipsychotics when associated with hyperprolactinemia may lead to decreased bone density in both female and male subjects.

5.18 Laboratory Tests

Fasting blood glucose testing and lipid profile at the beginning of, and periodically during, treatment is recommended [see Warnings and Precautions (5.12), and Patient Counseling Information (17.9)].

ZYPREXA RELPREVV database.

Since olanzapine has the potential to impair judgment, thinking, or motor skills, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that olanzapine therapy does not affect them adversely. However, due to the risk of post-injection delirium/sedation syndrome, patients should not drive or operate heavy machinery for the remainder of the day of each injection [see Dosage and Administration (2.1), Warnings and Precautions (5.1), and Patient Counseling Information (17.9)].

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Reference ID: 3675779

In a 24-week randomized, double-blind, fixed-dose study comparing 3 doses of ZYPREXA RELPREVV in patients with schizophrenia, statistically significant differences among dose groups were observed in the below safety outcomes (Table 10) [see Warnings and Precautions (5.5, 5.17)].

<table>
<thead>
<tr>
<th>Weight: mean change in kg (N)</th>
<th>Placebo (N=100)</th>
<th>150 mg/2 weeks (N=100)</th>
<th>405 mg/4 weeks (N=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.63 ± 14.0</td>
<td>5.61 ± 16.2</td>
<td>4.36 ± 17.4</td>
<td></td>
</tr>
<tr>
<td>p&lt;0.05 versus 300 mg/2 weeks ZYPREXA RELPREVV; pairwise p-values.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Dose Dependency of Adverse Reactions in Short-Term, Placebo-Controlled Trials

Extrapyramidal Symptoms: The following table enumerates the percentage of patients with treatment-emergent extrapyramidal symptoms as assessed by categorical analyses of formal rating scales during acute therapy in a controlled clinical trial comparing oral olanzapine at 3 fixed doses with placebo in the treatment of schizophrenia in a 6-week trial.

<table>
<thead>
<tr>
<th>Percentage of Patients Reporting Event</th>
<th>Placebo (N=100)</th>
<th>Olanzapine 5 ± 2.5 mg/day (N=100)</th>
<th>Olanzapine 10 ± 2.5 mg/day (N=100)</th>
<th>Olanzapine 15 ± 2.5 mg/day (N=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyskinesia</td>
<td>17%</td>
<td>20%</td>
<td>24%</td>
<td>25%</td>
</tr>
<tr>
<td>Parkinsonism</td>
<td>3%</td>
<td>4%</td>
<td>6%</td>
<td>8%</td>
</tr>
<tr>
<td>Akathisia</td>
<td>6%</td>
<td>8%</td>
<td>10%</td>
<td>12%</td>
</tr>
<tr>
<td>Dystonia</td>
<td>2%</td>
<td>3%</td>
<td>4%</td>
<td>5%</td>
</tr>
</tbody>
</table>

Differences among Fixed-Dose Groups Observed in Olanzapine Clinical Trials

In a single 8-week randomized, double-blind, fixed-dose study comparing 10 (N=199), 20 (N=200), and 40 (N=200) mg/day of oral olanzapine in patients with schizophrenia or schizoaffective disorder, differences among 3 dose groups were observed for the following safety outcomes: weight gain, prolactin elevation, fatigue and dysphoria. Mean baseline to endpoint increase in weight (10 mg/day: 1.9 kg; 20 mg/day: 2.3 kg; 40 mg/day: 3.0 kg) was observed with significant differences between 10 vs 40 and 20 vs 40 mg/day. Incidence of treatment-emergent prolactin elevation >24.2 ng/mL (female) or >18.7 ng/mL (male) at any time during the trial (10 mg/day: 31%; 20 mg/day: 42.7%; 40 mg/day: 61.1%) with significant differences between 10 vs 40 and 20 vs 40 mg/day, fatigue (10 mg/day: 1.5%; 20 mg/day: 2.1% 40 mg/day: 6.6%) with significant differences between 10 vs 40 and 20 vs 40 mg/day; and dyskinesia (10 mg/day: 2.6%; 20 mg/day: 1.6%; 40 mg/day: 6.6%) with significant differences between 20 vs 40 mg, was observed.

Differences among Fixed-Dose Groups Observed in Oral Olanzapine Clinical Trials

In a single 8-week randomized, double-blind, fixed-dose study comparing 10 (N=199), 20 (N=200), and 40 (N=200) mg/day of oral olanzapine in patients with schizophrenia or schizoaffective disorder, differences among 3 dose groups were observed for the following safety outcomes: weight gain, prolactin elevation, fatigue and dysphoria. Mean baseline to endpoint increase in weight (10 mg/day: 1.9 kg; 20 mg/day: 2.3 kg; 40 mg/day: 3.0 kg) was observed with significant differences between 10 vs 40 and 20 vs 40 mg/day. Incidence of treatment-emergent prolactin elevation >24.2 ng/mL (female) or >18.7 ng/mL (male) at any time during the trial (10 mg/day: 31%; 20 mg/day: 42.7%; 40 mg/day: 61.1%) with significant differences between 10 vs 40 and 20 vs 40 mg/day, fatigue (10 mg/day: 1.5%; 20 mg/day: 2.1% 40 mg/day: 6.6%) with significant differences between 10 vs 40 and 20 vs 40 mg/day; and dyskinesia (10 mg/day: 2.6%; 20 mg/day: 1.6%; 40 mg/day: 6.6%) with significant differences between 20 vs 40 mg, was observed.
Commonly Observed Adverse Reactions During the Clinical Trial Evaluation of Oral Olanzapine

In clinical trials of oral olanzapine monotherapy for the treatment of schizophrenia in adults, treatment-emergent adverse reactions with an incidence of 5% or greater in the olanzapine treatment arm and at least twice that of placebo were: hypotension, constipation, weight gain, dizziness, personality disorder, and akathisia.

Other Adverse Reactions Observed During the Clinical Trial Evaluation of Oral Olanzapine

Following is a list of treatment-emergent adverse reactions reported by patients treated with oral olanzapine (at multiple doses ≥1 mg/day) in clinical trials. This listing is not intended to include reactions (1) already listed in previous tables or elsewhere in labeling, (2) for which a drug cause was remote, (3) which were not considered to be drug-related, (4) which were not considered to have significant clinical implications, or (5) which occurred at a rate equal to or less than placebo. Reactions are classified by body system using the following definitions: frequent adverse reactions are those occurring in at least 1/100 patients; infrequent adverse reactions are those occurring in 1/100 to 1/1000 patients; rare adverse reactions are those occurring in fewer than 1/1000 patients.

Body as a Whole — Infrequent: chills, face edema, photosensitivity reaction, suicide attempt; Rare: chills and fever, hangover effect, sudden death.

Cardiovascular System — Infrequent: cerebrovascular accident, vasodilatation.

Digestive System — Infrequent: nausea and vomiting, tongue edema; Rare: ileus, intestinal obstruction, liver fatty deposit.

Hemic and Lympathytic System — Infrequent: leukenmia, thrombocytopenia.

Metabolic and Nutritional Disorders — Infrequent: alkaline phosphatase increased, bilirubinemia, hypoproteinemia.

Musculoskeletal System — Rare: osteoporosis.

Nervous System — Infrequent: ataxia, dysphoria, libido decreased, stupor; Rare: coma.

Respiratory System — Infrequent: epistaxis; Rare: lung edema.

Skin and Appendages — Infrequent: alopecia.

Special Senses — Infrequent: abnormality of accommodation, dry eyes; Rare: mydriasis.

Urogenital System — Infrequent: amenorrhea, breast pain, decreased menstruation, impotence, increased menstruation, menorrhagia, metrorrhagia, polyuria, urinary frequency, urinary retention, urinary urgency, urination impaired.

These terms represent serious adverse events but do not meet the definition for adverse drug reactions. They are included here because of their seriousness.

Adjusted for gender.

6.2 Vital Signs and Laboratory Studies Laboratory Changes

ZYPREXA RELPREVV in Adults: Statistically significant within group mean changes for ZYPREXA RELPREVV, which were also significantly different from placebo, were observed for the following: eosinophils, monocytes, cholesterol, low-density lipoprotein (LDL), triglycerides, and direct bilirubin. There were no statistically significant differences between ZYPREXA RELPREVV and placebo in the incidence of potentially clinically significant changes in any of the laboratory values studied.

Statistically significant within group mean changes for ZYPREXA RELPREVV, which were also significantly different from oral olanzapine (in a 24-week double-blind study), were observed for the following: gamma-glutamyltransferase (GGT), alkaline phosphatase, and total bilirubin. There was a statistically significant difference between ZYPREXA RELPREVV and oral olanzapine in the incidence of treatment-emergent low platelet count (6% ZYPREXA RELPREVV vs 1% oral olanzapine); and low total bilirubin (2.8% ZYPREXA RELPREVV vs 0.7% for oral olanzapine). There was a statistically significant difference between ZYPREXA RELPREVV and oral olanzapine in potentially clinically significant changes for high leukocyte count (6% ZYPREXA RELPREVV vs 1% oral olanzapine).

Changes inaminotransferases observed with ZYPREXA RELPREVV treatment were similar to those reported with ZYPREXA treatment. In placebo-controlled ZYPREXA RELPREVV studies, clinically significant ALT elevations ≤3 times the upper limit of the normal range were observed in 2.7% (5/188) of patients treated with ZYPREXA RELPREVV and oral olanzapine compared to 3.2% (3/94) of the placebo patients. None of these patients experienced jaundice.

In 3 of these patients, liver enzymes reverted to the normal range despite continued treatment, and in 5 cases enzymes values decreased, but were still above the normal range at the end of therapy.

Within the ZYPREXA RELPREVV database of 1196 patients with baseline ALT ≤50 IU/L, the incidence of ALT elevation to >200 IU/L, which was 0.6%. None of these patients experienced jaundice or other symptoms attributable to liver impairment and most had transient changes that tended to normalize while ZYPREXA RELPREVV treatment was continued.

Glucose Monitored in Adults: An assessment of the premarketing experience for oral olanzapine revealed an association with asymptomatic increases in ALT AST, and GGT. Within the original premarketing database of about 2400 adult patients with baseline AST ≤50 IU/L, the incidence of ALT elevations to >200 IU/L was 2% (50/2381). None of these patients experienced jaundice or other symptoms attributable to liver impairment and most had transient changes that tended to normalize while ZYPREXA RELPREVV treatment was continued.

Olanzapine Monotherapy in Adults: Between-group comparisons for pooled placebo-controlled studies of olanzapine monotherapy at 5-15 mg/day revealed no significant differences on ECG changes. Between-group comparisons for pooled placebo-controlled trials revealed no significant oral olanzapine/placebo differences in the proportions of patients experiencing potentially important changes in ECG parameters, including QT, QTc, and PR intervals. Oral olanzapine use was associated with a mean increase in heart rate of 2.4 beats per minute compared to no change among placebo patients. This slight tendency to tachycardia may be related to olanzapine’s potential for inducing orthostatic hypotension [see Warnings and Precautions (5.11)].

6.3 Postmarketing Experience

Adverse reactions reported in the market introduction that were temporally but not necessarily causally related to ZYPREXA therapy include the following: allergic reaction (e.g., anaphylactoid reaction, angioneurodema, pruritis or urticaria), diabetic coma, diabetic ketoadiabetes, discontinuation reaction (diaphoresis, nausea, or vomiting), jaundice, neutropenia, pancreatitis, pruritis, rash, rhabdomyolysis, and venous thromboembolic disorder (including pulmonary embolism and deep venous thrombosis). Random cholesterole levels of ≥240 mg/dl and random triglyceride levels of ≥300 mg/dl have been reported.

7. Drug Interactions

7.1 Carbohydrate Metabolism — Co-administration of olanzapine with metformin may increase the blood level of metformin and cause clinical manifestations of lactic acidosis. Co-administration of olanzapine with tolbutamide or acetohexamide may increase their blood levels.

7.2 CNS Drugs — Given the CNS effects of olanzapine, caution should be used if olanzapine is taken in combination with other centrally acting drugs and alcohol.

7.3 Antihypertensive Agents — Olanzapine, because of its potential for inducing hypotension, may enhance the effects of certain antihypertensive agents.

7.4 Laxatives and Diapering Agents — Olanzapine may antagonize the effects of levodopa and dopamine agonists.

7.5 Psychotropic Drugs — With concurrent administration of another psychotropic agent, the plasma concentration of olanzapine may increase or decrease.

7.6 Drug Interactions with Other Non-CNS Drugs — Drug interactions with olanzapine may occur with orally administered medications not primarily intended to alter CNS function.

7.7 Alcohol — Multiple doses of olanzapine (10 mg for 2 days) did not affect the steady-state plasma concentrations of valproate. Therefore, concomitant olanzapine administration does not require dosage adjustment of valproate.

7.8 Antipsychotics — Concomitant use of olanzapine and another antipsychotic may increase the plasma levels of each drug.

7.9 Other — Concomitant use of olanzapine with other drugs may increase the plasma levels of olanzapine.

7.10 Cardiovascular — Concomitant use of olanzapine and other cardiovascular drugs may increase the plasma levels of olanzapine.

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy Teratogenic Effects. Pregnancy Category C — Oral olanzapine co-administration during clinical trials with ZYPREXA RELPREVV, including 1 result in a normal birth and 3 therapeutic abortions. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if the potential benefits justify the potential risk to the fetus.

Neonatal Effects — Neonates exposed to antipsychotic drugs (including olanzapine) during the third trimester of pregnancy are at risk for drug withdrawal symptoms following delivery. There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress and feeding disorder in these neonates. These complications have varied in severity; while in some cases symptoms have been self-limited, in other cases neonates have required intensive care unit support and prolonged hospitalization.

There are no adequate and well-controlled trials with olanzapine in pregnant females. Four pregnancies were observed during clinical trials with ZYPREXA RELPREVV, including 1 result in a normal birth and 3 therapeutic abortions. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if the potential benefits justify the potential risk to the fetus.

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Reference ID: 3657797
ZYPREXA RELPREVV should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

8.2 Labor and Delivery
The effect of olanzapine on labor and delivery in humans is unknown. Parturition in ruminants was not affected by olanzapine.

8.3 Nursing Mothers
In an oral olanzapine study in lactating, healthy women, olanzapine was excreted in breast milk. Mean infant dose at steady state was estimated to be 1.8% of the maternal olanzapine dose. It is recommended that women receiving ZYPREXA RELPREVV should not breast-feed.

8.4 Pediatric Use
Safety and effectiveness of ZYPREXA RELPREVV in children and adolescent patients have not been established. (see Warnings and Precautions (5.6, 5.7, 5.8).)

Compared to patients from adult clinical trials, adolescents treated with oral ZYPREXA were likely to gain more weight, experience increased sedation, and have greater increases in total cholesterol, triglycerides, LDL cholesterol, prolactin and hepatic aminotransferase levels.

8.5 Geriatric Use
Clinical studies of ZYPREXA RELPREVV did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. In the premarketing clinical studies with oral olanzapine, there was no indication of any different tolerability of olanzapine in elderly patients compared to younger patients with schizophrenia. Oral olanzapine studies in elderly patients with dementia-related psychosis have suggested that there may be a different tolerability profile in this population compared to younger patients with schizophrenia. Elderly patients with dementia-related psychosis treated with olanzapine are at an increased risk of death compared to placebo. In placebo-controlled studies of olanzapine in elderly patients with dementia-related psychosis, there was a higher incidence of cerebrovascular adverse events (e.g., stroke, transient ischemic attack) in patients treated with olanzapine compared to patients treated with placebo. Olanzapine is not approved for the treatment of patients with dementia-related psychosis. Also, the presence of factors that might decrease pharmacokinetic clearance or increase the pharmacodynamic response to olanzapine should lead to consideration of a lower starting dose for any geriatric patient (see Boxed Warning, Warnings and Precautions (5.3), and Dosage and Administration (2.1)).

9 DRUG ABUSE AND DEPENDENCE
9.3 Dependence
In studies prospectively designed to assess abuse and dependence potential, olanzapine was shown to have acute depressive CNS effects but little or no potential of abuse or physical dependence in rats administered oral doses up to 15 times the maximum recommended human daily oral dose (20 mg) and rhesus monkeys administered oral doses up to 8 times the maximum recommended human daily oral dose on a mg/m² basis.

Olanzapine has been systematically studied in humans for its potential for abuse, tolerance, or physical dependence. Because ZYPREXA RELPREVV is to be administered by healthcare professionals, the potential for misuse or abuse by patients is low.

10 OVERDOSAGE
10.1 Human Experience
During premarketing clinical studies of ZYPREXA RELPREVV, adverse reactions that presented with signs and symptoms consistent with olanzapine overdose, in particular, sedation (including coma) and/or delirium, were reported in patients following an injection of ZYPREXA RELPREVV (see [Boxed Warning and Dosage and Administration (2.1)]. These reactions occurred in <0.1% of patients and in approximately 2% of patients who received injections for up to 46 months. These reactions were correlated with an unintentional rapid increase in serum olanzapine concentrations to supra-therapeutic ranges in some cases. While a rapid and greater than expected increase in serum olanzapine concentration has been observed in some patients with these reactions, the exact mechanism by which the drug was unintentionally introduced into the blood stream is not known. Clinical signs and symptoms included dizziness, confusion, disorientation, slurred speech, altered gait, difficulty ambulating, weakness, agitation, extrapyramidal symptoms, hypotension, convulsion, and reduced level of consciousness ranging from mild sedation to coma. Time after injection to event ranged from soon after injection to greater than 3 hours after injection. The majority of patients were hospitalized and some required supportive care, including intubation, in several cases. All patients had largely recovered by 72 hours. The risk of an event is the same at each injection, so the risk per patient is cumulative (i.e., increases with the number of injections) (see [Warnings and Precautions (5.1)].

In postmarketing reports of overdose with oral olanzapine alone, symptoms have been reported in the majority of cases. In symptomatic patients, symptoms with ≥10% incidence included agitation/aggressiveness, dysarthria, tachycardia, various extrapyramidal symptoms, and reduced level of consciousness ranging from sedation to coma. Among less commonly reported symptoms were the following potentially medically serious reactions: aspiration, cardiopulmonary arrest, cardiac arrhythmias (such as supraventricular tachycardia and 1 patient experiencing sinus pause with spontaneous resumption of normal rhythm), delirium, possible neuroleptic malignant syndrome, respiratory depression/arrest, convulsion, hypertension, and hypotension. Eli Lilly and Company has received reports of fatality in association with overdose of oral olanzapine alone. In 1 case of death, the amount of acutely ingested oral olanzapine was reported to be possibly as low as 450 mg of olanzapine; however, in another case, a patient was reported to survive an acute olanzapine ingestion of approximately 2 g of oral olanzapine.

10.2 Management of Overdose
Post-injection delirium/sedation syndrome may occur with each injection of ZYPREXA RELPREVV. Signs and symptoms consistent with olanzapine overdose have been observed, and access to emergency response services must be readily available for safe use (see Boxed Warning and Warnings and Precautions (5.1)).

There is no specific antidote to olanzapine. Therefore, appropriate supportive measures should be initiated. Hypotension and circulatory collapse should be treated with appropriate measures such as intravenous fluids and/or sympathomimetic agents. (Do not use epinephrine, dopamine, or other sympathomimetics with beta-stimulating effects, since beta stimulation may worsen hypotension in the setting of olanzapine-induced alpha blocking activity.) Respiratory support, including ventilation, may be required. Close medical supervision and monitoring should continue to the patient’s recovery.

The possibility of multiple drug involvement should be considered. In case of acute overdosage, establish and maintain an airway and ensure adequate oxygenation and ventilation, which may include intubation. The possibility of dehydration, seizures, or dysrhythmic reaction of the head and neck following overdose may create a risk of aspiration with induced emesis. Cardiovascular monitoring should commence immediately and should include continuous electrocardiographic monitoring to detect possible arrhythmias.

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ZYPREXA RELPREVV (olanzapine) For Extended Release Injectable Suspension

Pharmacokinetic Impact of Switching to ZYPREXA RELPREVV from Oral Olanzapine — The switch from oral olanzapine to ZYPREXA RELPREVV changes the pharmacokinetics from an elimination-rate-controlled to an absorption-rate-controlled process. The switch to ZYPREXA RELPREVV may require treatment for a period of approximately 3 months to re-establish steady-state conditions. Initial treatment with ZYPREXA RELPREVV is recommended. Concomitant use of antacid or buffered oral antacids, which may alter the pH of the stomach, is not recommended. Due to the high incidence of early mortalities in males of the 30/20 mg/kg/day group. The incidence of mammary gland hyperplasia in female rats dosed at ≥4 mg/kg/day (0.5 and 2 times the maximum recommended human daily oral dose on a mg/m² basis, respectively). Discontinuation of olanzapine treatment reversed the effects on male mating performance. In male dogs treated with olanzapine, the precoital period was increased by 2.5 times the maximum recommended human daily oral dose on a mg/m² basis). Diestrous was prolonged and estrous delayed at 1.1 mg/kg (0.6 times the maximum recommended human daily oral dose on a mg/m² basis); therefore, olanzapine must be used in dosing the elderly, especially if there are other factors that might additively influence drug clearance of olanzapine, a study of the effect of impaired liver function in subjects (n=6) with clinically relevant drug metabolism and/or pharmacodynamic sensitivity should be used in dosing the elderly, especially if there are other factors that might additively influence drug clearance of olanzapine.

Geriatric — In a study involving 24 healthy subjects, the mean elimination half-life of orally administered olanzapine was about 1.5 times greater in elderly (≥65 years) than in nonelderly subjects (<65 years). Caution should be used in dosing the elderly, especially if there are other factors that might additively influence drug metabolism and/or pharmacodynamic sensitivity should be used in dosing the elderly, especially if there are other factors that might additively influence drug clearance of olanzapine.

Racial — In vivo studies of orally administered olanzapine have shown that exposures are similar among Japanese, Chinese and Caucasians, especially after normalization for body weight differences. Dosage modifications for race are, therefore, not recommended.

13.2 Animal Toxicology and/or Pharmacology

In animal studies with olanzapine, the principal hematologic findings were reversible peripheral cytopenias in individual dogs treated at 10 mg/kg (17 times the maximum recommended human daily oral dose on a mg/m² basis), dose-related decreases in lymphocytes and neutrophils in mice, and lymphopenia in rats. A few dogs treated with 10 mg/kg developed reversible neutropenia and/or reversible hypertensive anemia between 1 and 10 months of treatment. Dose-related decreases in lymphocytes and neutrophils were seen in mice given doses of 10 mg/kg (equal to 2 times the maximum recommended human daily oral dose on a mg/m² basis) in studies of 3 months’ duration. Non-specific lymphopenia, with decreased body weight gain, occurred in rats receiving 22.5 mg/kg (11 times the maximum recommended human daily oral dose on a mg/m² basis) for 3 months or 16 mg/kg (8 times the maximum recommended human daily oral dose on a mg/m² basis) for 6 or 12 months. No evidence of bone marrow cytotoxicity was found in any of the species examined. Bone marrows were normocellular or hypocellular, indicating that the reductions in circulating blood cells were probably due to peripheral (non-marrow) factors.

14. CLINICAL STUDIES

14.1 Schizophrenia

The short-term effectiveness of ZYPREXA RELPREVV was established in an 8-week, placebo-controlled trial in adult patients (n=604) who were experiencing psychosomatic symptoms and met DSM-IV or DSM-IV-TR criteria for schizophrenia. Patients were randomized to receive injections of ZYPREXA RELPREVV 210 mg every 2 weeks, ZYPREXA RELPREVV 405 mg every 4 weeks, ZYPREXA RELPREVV 300 mg every 2 weeks, or placebo every 2 weeks. Patients were discontinued from their previous antipsychotics and underwent a 2-7 day washout period. No oral antipsychotic supplementation was allowed throughout the trial. The primary efficacy measure was change from baseline to endpoint in Positive and Negative Symptom Scale (PANSS) score (mean total baseline total PANSS score 101). Total PANSS scores showed statistically significant improvement from baseline to endpoint with each dose of ZYPREXA RELPREVV (210 mg every 2 weeks, 405 mg every 4 weeks, and 300 mg every 2 weeks) as compared to placebo. The effectiveness of ZYPREXA RELPREVV in the treatment of schizoaffective disorder is further supported by the established effectiveness of the oral formulation of olanzapine.

A longer-term trial enrolled patients with schizophrenia (n=1065) who had remained stable for 4 to 8 weeks on open-label treatment with oral olanzapine (mean baseline total PANSS score 56) and were then randomized to continue their current oral olanzapine dose (10, 15, or 20 mg/day); or to ZYPREXA RELPREVV 150 mg every 2 weeks, 4 weeks, or 25 mg every 2 weeks, 4 weeks, or 25 mg every 4 weeks. No oral antipsychotic supplementation was allowed throughout the trial. The primary efficacy measure was time to exacerbation of symptoms of schizophrenia defined in terms of increases in Brief Psychiatric Rating Scale (BPRS) positive symptoms or hospitalization. ZYPREXA RELPREVV doses of 150 mg every 2 weeks, 405 mg every 4 weeks, and 300 mg every 2 weeks were each statistically significantly superior to low dose ZYPREXA RELPREVV (45 mg every 4 weeks).
17.2 Post-Injection Delirium/Sedation Syndrome

During premarketing clinical studies, reactions that presented with signs and symptoms consistent with olanzapine overdoses have been reported in patients following an injection of ZYPREXA RELPREVY. It is mandatory that patients be entered in the ZYPREXA RELPREVY Patient Care Program to receive ZYPREXA RELPREVY treatment. Patients should be advised of the risk of post-injection delirium/sedation syndrome each time they receive an injection [see Warnings and Precautions (5.1, 5.2)]. Patients and caregivers should be advised that after each ZYPREXA RELPREVY injection, patients must be observed at the healthcare facility for at least 2 hours and must be accompanied to their destination upon leaving the facility. The Medication Guide should be distributed each time patients receive an injection.

17.3 Elderly Patients with Dementia-Related Psychosis—Increased Mortality and Cardiovascular Adverse Events (CVAEs), Including Stroke

Patients and caregivers should be advised that elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Patients and caregivers should be advised that elderly patients with dementia-related psychosis treated with ZYPREXA had a significantly higher incidence of cardiovascular adverse events (e.g., stroke, transient ischemic attack) compared with placebo. ZYPREXA RELPREVY is not approved for elderly patients with dementia-related psychosis [see Boxed Warning and Warnings and Precautions (5.2)].

17.4 Neuroleptic Malignant Syndrome (NMS)

Patients and caregivers should be counseled that a potentially fatal symptom complex sometimes referred to as NMS has been reported in association with administration of antipsychotic drugs, including ZYPREXA. Signs and symptoms of NMS include hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmias) [see Warnings and Precautions (5.5)].

17.5 Hyperglycemia

Patients should be advised of the potential risk of hyperglycemia-related adverse reactions related to ZYPREXA RELPREVY. Patients should be monitored regularly for worsening of glucose control. Patients who have diabetes should follow their doctor's instructions about how often to check their blood sugar while taking ZYPREXA RELPREVY [see Warnings and Precautions (5.8)].

17.6 Hypertension

Patients should be counseled that hypertension has occurred during treatment with ZYPREXA RELPREVY. Patients should have their blood pressure monitored regularly [see Warnings and Precautions (5.7)].

17.7 Weight Gain

Patients should be counseled that weight gain has occurred during treatment with ZYPREXA RELPREVY. Patients should have their weight monitored regularly [see Warnings and Precautions (5.8)].

17.8 Orthostatic Hypotension

Patients should be advised of the risk of orthostatic hypotension, and in association with the use of concomitant drugs that may potentiate the orthostatic effect of ZYPREXA RELPREVY, e.g., diuretics or alcohol [see Warnings and Precautions (5.9) and Drug Interactions (7)]. Patients should be advised to change positions carefully to help prevent orthostatic hypotension, and to lie down if they feel dizzy or faint, until they feel better. Patients should be advised to call their doctor if they experience any of the following signs and symptoms associated with orthostatic hypotension: dizziness, faint or slow heart beat, or fainting.

17.9 Potential for Cognitive and Motor Impairment

Because ZYPREXA RELPREVY has the potential to impair judgment, thinking, or motor skills, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that ZYPREXA RELPREVY therapy does not affect them adversely. Additionally, due to the risk of post-injection delirium/sedation syndrome, patients should not drive or operate heavy machinery for the remainder of the day of each injection [see Dosage and Administration (2.1) and Warnings and Precautions (5.1, 5.4)].

17.10 Body Temperature Regulation

Patients should be advised regarding appropriate care in avoiding overheating and dehydration. Patients should be advised to call their doctor right away if they become severely ill and have some or all of these symptoms of dehydration: sweating too much or not at all, dry mouth, feeling very hot, feeling thirsty, not able to produce urine [see Warnings and Precautions (5.15)].

17.11 Concomitant Medication

Patients should be advised to inform their physicians if they are taking, or plan to take, ZYPREXA or Symbicort® (budesonide/formoterol fumarate combination). Patients should also be advised to inform their physicians if they are taking, plan to take, or have stopped taking any prescription or over-the-counter drugs, including herbal supplements, since there is a potential for interactions [see Drug Interactions (7)].

17.12 Alcohol

Patients should be advised to avoid alcohol while taking ZYPREXA RELPREVY [see Drug Interactions (7.1)].

17.13 Use in Specific Populations

Pregnancy — Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy with ZYPREXA RELPREVY [see Use in Specific Populations (8.1)].

Nursing Mothers — Patients should be advised not to breast-feed an infant if they are taking ZYPREXA RELPREVY [see Use in Specific Populations (8.3)].

Pediatric Use — Safety and effectiveness of ZYPREXA RELPREVY in patients under 18 years have not been established [see Use in Specific Populations (8.4)].

Literature revised July 5, 2011

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PV 5924 AMP
ZYPREXA RELPREVY (olanzapine) For Extended Release Injectable Suspension  PV 5924 AMP
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Medication Guide

ZYPREXA® RELPREVV™ (zy-PREX-a REL-prev)
(olanzapine)

For Extended Release Injectable Suspension

Read the Medication Guide that comes with ZYPREXA RELPREVV before you start taking it and each time before you get an injection. There may be new information. This Medication Guide does not take the place of talking to your doctor about your medical condition or treatment. Talk with your doctor if there is something you do not understand or you want to learn more about ZYPREXA RELPREVV.

What is the most important information I should know about ZYPREXA RELPREVV?

Before you receive ZYPREXA RELPREVV treatment you must:
• understand the risks and benefits of ZYPREXA RELPREVV treatment. Your doctor will talk to you about the risks and benefits of ZYPREXA RELPREVV treatment.
• register in the ZYPREXA RELPREVV Patient Care Program. You must agree to the rules of the ZYPREXA RELPREVV Patient Care Program before you register.

ZYPREXA RELPREVV may cause serious side effects, including:
1. Post-injection Delirium Sedation Syndrome (PDSS).
2. Increased risk of death in elderly people who are confused, have memory loss and have lost touch with reality (dementia-related psychosis).
3. High blood sugar (hyperglycemia).
4. High fat levels in your blood (increased cholesterol and triglycerides), especially in teenagers age 13 to 17.
5. Weight gain, especially in teenagers age 13 to 17.

These serious side effects are described below.

1. Post-injection Delirium Sedation Syndrome (PDSS). PDSS is a serious problem that can happen after you get a ZYPREXA RELPREVV injection if the medicine gets in your blood too fast. This problem usually happens within 3 hours after you receive ZYPREXA RELPREVV. If the medicine gets in your blood too fast, you may have some of the following symptoms:
   • feel more sleepy than usual
   • feel dizzy
   • feel confused or disoriented
   • trouble talking or walking
   • muscles feel stiff or shaking
   • feel weak
   • feel grouchy or angry
   • feel nervous or anxious
   • higher blood pressure
   • seizures (convulsions)
   • pass out (become unconscious or coma)

   You will need to stay at the clinic where you receive the injection for at least 3 hours so your doctor can make sure you do not have symptoms of PDSS. When you leave the clinic someone must be with you. If you have symptoms of PDSS after you leave the clinic, get medical help or go to an emergency room right away.

2. Increased risk of death in elderly people who are confused, have memory loss and have lost touch with reality (dementia-related psychosis). ZYPREXA RELPREVV is not approved for treating psychosis in elderly people with dementia.

3. High blood sugar (hyperglycemia). High blood sugar can happen if you have diabetes already or if you have never had diabetes. High blood sugar could lead to:
   • a build up of acid in your blood due to ketones (ketoacidosis)
   • coma
   • death

   Your doctor should do tests to check your blood sugar before you start taking ZYPREXA RELPREVV and during treatment. In people who do not have diabetes, sometimes high blood sugar goes away when ZYPREXA RELPREVV is stopped. People with diabetes and some people who did not have diabetes before taking ZYPREXA RELPREVV need to take medicine for high blood sugar even after they stop taking ZYPREXA RELPREVV.

   If you have diabetes, follow your doctor’s instructions about how often to check your blood sugar while taking ZYPREXA RELPREVV.

4. High fat levels in your blood (cholesterol and triglycerides). High fat levels may happen in people treated with ZYPREXA RELPREVV, especially in teenagers (13 to 17 years old). ZYPREXA RELPREVV is not approved in patients less than 18 years old. You may not have any symptoms, so your doctor should do blood tests to check your cholesterol and triglyceride levels before you start taking ZYPREXA RELPREVV and during treatment.

5. Weight gain. Weight gain is very common in people who take ZYPREXA RELPREVV. Teenagers (13 to 17 years old) are more likely to gain weight and to gain more weight than adults. ZYPREXA RELPREVV is not approved in patients less than 18 years old. Some people may gain a lot of weight while taking ZYPREXA RELPREVV, so you and your doctor should check your weight regularly. Talk to your doctor about ways to control weight gain, such as eating a healthy, balanced diet, and exercising.

What is ZYPREXA RELPREVV?

ZYPREXA RELPREVV is a long-acting prescription medicine given by injection and used to treat schizophrenia in adults. The symptoms of schizophrenia include:
• hearing voices
• seeing things that are not there
• having beliefs that are not true
• being suspicious or withdrawn

Some of your symptoms of schizophrenia may improve with treatment with ZYPREXA RELPREVV. If you do not think you are getting better, call your doctor. It is not known if ZYPREXA RELPREVV is safe and effective in children under 18 years of age.

What should I tell my doctor before taking ZYPREXA RELPREVV?

ZYPREXA RELPREVV may not be right for you. Before starting ZYPREXA RELPREVV, tell your doctor if you have or had:
• heart problems
• seizures
• diabetes or high blood sugar levels (hyperglycemia)
• high cholesterol or triglyceride levels in your blood
• liver problems
• low or high blood pressure
• strokes or “mini-strokes” also called transient ischemic attacks (TIAs)
• Alzheimer’s disease
• narrow-angle glaucoma
• enlarged prostate in men
• bowel obstruction
• breast cancer
thoughts of suicide or hurting yourself
• any other medical condition
• are pregnant or plan to become pregnant. It is not known if ZYPREXA RELPREV will harm your unborn baby.
• are breast-feeding or plan to breast-feed. ZYPREXA RELPREV can pass into your breast milk and may harm your baby. You should not breast-feed while taking ZYPREXA RELPREV. Talk to your doctor about the best way to feed your baby if you take ZYPREXA RELPREV.

Tell your doctor if you exercise a lot or are in hot places often.
The symptoms of schizophrenia may include thoughts of suicide or of hurting yourself or others. If you have these thoughts at any time, tell your doctor or go to an emergency room right away.

Tell your doctor about all the medicines that you take, including prescription and nonprescription medicines, vitamins, and herbal supplements. ZYPREXA RELPREV and some medicines may interact with each other and may not work as well, or cause possible serious side effects. Your doctor can tell you if it is safe to take ZYPREXA RELPREV with your other medicines. Do not start or stop any medicine while taking ZYPREXA RELPREV without talking to your doctor first.

How should I receive ZYPREXA RELPREV?
• ZYPREXA RELPREV will be injected into the muscle in your buttock (gluteus) by your doctor or nurse at the clinic.
• After receiving ZYPREXA RELPREV, you will need to stay at the clinic for at least 3 hours.
• When you leave the clinic, someone must be with you.
• Call your doctor if you do not think you are getting better or have any concerns about your condition while taking ZYPREXA RELPREV.

What should I avoid while receiving ZYPREXA RELPREV?
• ZYPREXA RELPREV can cause sleepiness and may affect your ability to make decisions, think clearly, or react quickly. Do not drive, operate heavy machinery, or do other dangerous activities until you know how ZYPREXA RELPREV affects you. You should not drive or operate heavy machinery for the rest of the day after each injection.
• Avoid drinking alcohol while taking ZYPREXA RELPREV. Drinking alcohol while you take ZYPREXA RELPREV may make you sleepier than if you take ZYPREXA RELPREV alone.

What are the possible side effects of ZYPREXA RELPREV?
Serious side effects may happen when you take ZYPREXA RELPREV, including:
• See “What is the most important information I should know about ZYPREXA RELPREV?”, which describes the risk of post-injection delirium sedation syndrome (PDSS), increased risk of death in elderly people with dementia-related psychosis and the risks of high blood sugar, high cholesterol and triglyceride levels, and weight gain.
• Increased incidence of stroke or “mini-strokes” called transient ischemic attacks (TIAs) in elderly people with dementia-related psychosis (elderly people who have lost touch with reality due to confusion and memory loss). ZYPREXA RELPREV is not approved for these patients.
• Neuroleptic Malignant Syndrome (NMS): NMS is a rare but very serious condition that can happen in people who take antipsychotic medicines, including ZYPREXA RELPREV. NMS can cause death and must be treated in a hospital. Call your doctor right away if you become severely ill and have any of these symptoms:
  • high fever
  • excessive sweating
  • rigid muscles
  • confusion
  • changes in your breathing, heartbeat, and blood pressure
• Tardive Dyskinesia: This condition causes body movements that keep happening and that you can not control. These movements usually affect the face and tongue. Tardive dyskinesia may not go away, even if you stop taking ZYPREXA RELPREV. It may also start after you stop taking ZYPREXA RELPREV. Tell your doctor if you get any body movements that you can not control.
• Decreased blood pressure when you change positions, with symptoms of dizziness, fast or slow heartbeat, or fainting.
• Difficulty swallowing, that can cause food or liquid to get into your lungs.
• Seizure: Tell your doctor if you have a seizure during treatment with ZYPREXA RELPREV.
• Problems with control of body temperature: You could become very hot, for instance when you exercise a lot or stay in an area that is very hot. It is important for you to drink water to avoid dehydration. Call your doctor right away if you become severely ill and have any of these symptoms of dehydration:
  • sweating too much or not at all
  • dry mouth
  • feeling very hot
  • feeling thirsty
  • not able to produce urine

Common side effects of ZYPREXA RELPREV include: headache, sleepiness or drowsiness, weight gain, dry mouth, diarrhea, nausea, common cold, eating more (increased appetite), vomiting, cough, back pain, or pain at the injection site.

Tell your doctor about any side effect that bothers you or that does not go away. These are not all the possible side effects with ZYPREXA RELPREV. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about ZYPREXA RELPREV
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide.

This Medication Guide summarizes the most important information about ZYPREXA RELPREV. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about ZYPREXA RELPREV that was written for healthcare professionals. For more information about ZYPREXA RELPREV call 1-800-Lilly-Rx (1-800-545-5979) or visit www.zyprexa-relprev.com.

What are the ingredients in ZYPREXA RELPREV?
Active ingredient: olanzapine
Inactive ingredients: carboxymethylcellulose sodium, mannitol, polysorbate 80, sodium hydroxide and/or hydrochloric acid for pH adjustment, and water for injection

This Medication Guide has been approved by the U.S. Food and Drug Administration.

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