Please see Prescribing Information for full details about the risks of ZYPREXA RELPREVV, including Boxed Warnings.
Enclosed Registration Forms Include:

► **Prescriber Registration**
   Enrolls the prescriber to treat patients with ZYPREXA RELPREVV.

► **Pharmacy Service Providers**
  ▪ **Pharmacy Registration**
    Enrolls the pharmacy to order and dispense ZYPREXA RELPREVV.
  ▪ **Buy and Bill Pharmacy Service Provider Registration**
    For prescribers who get product through standard buy and bill procedures, this form enrolls the prescriber as a Pharmacy Service Provider. **NOTE: Prescribers intending to buy and bill must complete both the Prescriber and Buy and Bill Pharmacy Service Provider Registration Forms.**

► **Patient Registration**
  Enrolls the patient to receive treatment with ZYPREXA RELPREVV.

► **Patient Registration Form – Patient Copy**
  Provides patient or caregiver a copy of attestations from the Patient Registration Form.

► **Healthcare Facility Registration**
  Enrolls the healthcare facility to administer ZYPREXA RELPREVV injections and monitor patients after each injection.
ZYPREXA RELPREVV Prescribing Information and Medication Guide

Patient Injection and PDSS Reporting Forms

**Single Patient Injection Form**
- Used to collect the data for a single patient after treatment administration of ZYPREXA RELPREVV.
- This form is to be sent to the ZYPREXA RELPREVV Patient Care Program Coordinating Center within 7 days after the patient’s injection.

**Multiple Patient Injection Form**
- Used when injections are administered to multiple patients on the same day at a given facility.
- This form is used to collect the data for multiple patients after treatment administration of ZYPREXA RELPREVV.
- This form is to be sent to the ZYPREXA RELPREVV Patient Care Program Coordinating Center within 7 days after the patients’ injections.

Patient injection data should only be completed either via the Single Patient Injection Form or the Multiple Patient Injection Form. Do not use both forms for an individual injection; this will result in duplicate reporting.

**Post-Injection Delirium/Sedation Syndrome (PDSS) Form**
- This form is used to collect the required data when a suspected PDSS event occurs after administration of ZYPREXA RELPREVV, either during the 3-hour observation period or any time thereafter. This form must be provided to the ZYPREXA RELPREVV Patient Care Program Coordinating Center within 24 hours of becoming aware of a suspected PDSS event.
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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.
ZYPREXA RELPREVV Patient Care Program Enrollment

Prescriber
- Reviews educational materials
- Submits enrollment form to ZYPREXA RELPREVV Patient Care Program Coordinating Center

Healthcare Facility
- Ensures staff are trained and facility can comply with conditions of safe use
- Submits enrollment form to ZYPREXA RELPREVV Patient Care Program Coordinating Center
- Receives & stores patient authorization notification

Patient
To enroll patient, prescriber:
- Reviews risks of ZYPREXA RELPREVV with patient
- Obtain signature of patient or legal guardian OR check box if court order of involuntary commitment
- Submits enrollment form to ZYPREXA RELPREVV Patient Care Program Coordinating Center
- Receives & stores patient authorization notification

Pharmacy Service Provider
- Reviews ZYPREXA RELPREVV Patient Care Program materials
- Ensures pharmacy staff are trained
- Submits enrollment form to ZYPREXA RELPREVV Patient Care Program Coordinating Center

ZYPREXA RELPREVV Patient Care Program Process Flow

Ordering
Enrolled Pharmacy Service Provider places ZYPREXA RELPREVV order with regular wholesaler

Pharmacy Service Provider receives ZYPREXA RELPREVV

Order is forwarded to Lilly/Specialty Distributor

Lilly/Specialty Distributor verifies Pharmacy Service Provider eligibility via the on-line system

ZYPREXA RELPREVV Patient Care Program Database and Coordinating Center

Dispensing
Prescriber submits prescription and patient identification number (PIN) to Pharmacy Service Provider

Pharmacy Service Provider confirms patient eligibility via the on-line system or via the Interactive Voice Response System (IVRS)

Patient eligibility is confirmed

Pharmacy Service Provider dispenses ZYPREXA RELPREVV to registered healthcare facility as indicated by the on-line system or IVRS and enters dispense date via the on-line system or via IVRS.

Treatment
Healthcare Professional/Prescriber
- administers ZYPREXA RELPREVV
- observes patient for 3 hours
- reports data for every injection and suspected PDSS event to the ZYPREXA RELPREVV Patient Care Program

* For the first prescription include the patient authorization notification
b If patient is not eligible, contact the ZYPREXA RELPREVV Patient Care Program Coordinating Center
c Data entry is required for patient to be eligible for refill
d PDSS = post-injection delirium/sedation syndrome

Key
- Prescriber Activities
- Healthcare Facility Activities
- Pharmacy Service Provider Activities
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.zyprexarelprevprogram.com
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.zyprexarelprevvprogram.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.
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.

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.zyprexarelprevprogram.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.
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
     - 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.zyprexarelprevvprogram.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.
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.

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).

### 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 vial 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.zyprexarelprevvprogram.com](http://www.zyprexarelprevvprogram.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.
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](http://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 vial 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 vial 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.
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 vial 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 RELPREVV 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 RELPREVV 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: ___________________________ MI: _____ Last Name: __________________

Preferred Method of Communication:  ☐ Email  ☐ Fax

Email: ___________________________________________________________

Phone: ___________________________ Fax: ___________________________

(If different from above) (If different from above)

PHARMACY SERVICE PROVIDER AGREEMENT

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 dispense, prior to the vial kit leaving the pharmacy.
• I understand that the ZYPREXA RELPREVV 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 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 facility.

Administrator Signature

Date: _______ – _______ – _______

* 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.zyprexarelprevvprogram.com

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HEALTHCARE FACILITY 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 healthcare facility may be enrolled in the ZYPREXA RELPREVV Patient Care Program.

HEALTHCARE FACILITY INFORMATION

- Enrolllment
- 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: ___________________________ (if different from above) |
| Email: _________________________________________________________________________________ |

| Delegate First Name: ___________________________ MI: _____ Last Name: ___________________________ |
| Facility Name: ___________________________________________________________________________
| Phone: ___________________________ Fax: ___________________________ (if different from above) |
| Email: _________________________________________________________________________________ |

| Delegate First Name: ___________________________ MI: _____ Last Name: ___________________________ |
| Facility Name: ___________________________________________________________________________
| Phone: ___________________________ Fax: ___________________________ (if different from above) |
| Email: _________________________________________________________________________________ |

| Delegate First Name: ___________________________ MI: _____ Last Name: ___________________________ |
| Facility Name: ___________________________________________________________________________
| Phone: ___________________________ Fax: ___________________________ (if different from above) |
| Email: _________________________________________________________________________________ |

| Delegate First Name: ___________________________ MI: _____ Last Name: ___________________________ |
| Facility Name: ___________________________________________________________________________
| Phone: ___________________________ Fax: ___________________________ (if different from above) |
| Email: _________________________________________________________________________________ |

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

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

• I have read and understand the ZYPREXA RELPREVV Patient Care Program Instructions Brochure;

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

• I will ensure that all appropriate 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 the health care setting has systems, protocols, or other measures to ensure that ZYPREXA RELPREVV 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 RELPREVV 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 RELPREVV Patient Care Program.

• I understand that the ZYPREXA RELPREVV 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 RELPREVV.

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

I understand that Lilly will regularly evaluate ZYPREXA RELPREVV 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 RELPREVV 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 RELPREVV to patients.

Authorized Healthcare Facility Representative Signature

Authorized Healthcare Facility Representative Name (print) _______________________________ Title ______________________________

Date: ___________ ___________ ___________

month day year

Please fax completed form to the ZYPREXA RELPREVV Patient Care Program at 1-877-772-9391.

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

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## 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 RELPREVV Patient Care Program Coordinating Center.

---

### Injection Facility Name:

[Blank]

### Date of Injection

[Blank]

### Patient Info.

<table>
<thead>
<tr>
<th>Patient No.: (PIN)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Patient Name:</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>First Name</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M.I.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Last Name</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date of Birth:</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>month</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>year</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>PDSS since last visit? (check one)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If Yes, has the prescriber been notified of the PDSS event?

<table>
<thead>
<tr>
<th>Patient Info.</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Time of Injection (24-hour clock)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>hour</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>minute</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose of Injection (check one)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>150 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>210 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>300 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>405 mg</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Other dose ___ mg</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Observed at least 3 hours post-injection? (check one)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>PDSS during onsite observation? (check one)</th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If Yes, has the prescriber been notified of the PDSS event?

<table>
<thead>
<tr>
<th>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)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Signature</th>
<th></th>
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<tbody>
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<td></td>
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<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Following the injection, was the patient accompanied from the facility? (check one)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not applicable, patient did not leave facility (in-patient)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Signature</th>
<th></th>
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<tbody>
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<td></td>
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<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Was the patient or legal guardian given a Medication Guide prior to this injection?</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

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**FAX 1-877-772-9391**  
**www.zyprexarelprevprogram.com**

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**Page 1 of 1**

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PATIENT INFORMATION

First Name: ___________________________________________ MI: _____ Last Name: ________________________________________

Date: ________________________________________________

PATIENT AGREEMENT

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

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

The ZYPREXA RELPREVV 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 RELPREVV Patient Care Program.

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

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

• Information from all patients in the ZYPREXA RELPREVV 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 RELPREVV 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 RELPREVV Patient Care Program registry to get ZYPREXA RELPREVV.

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

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

• 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 RELPREVV.

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

You may stop participating in the ZYPREXA RELPREVV 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 RELPREVV Patient Care Program except to answer safety questions. The ZYPREXA RELPREVV Patient Care Program will still use information that was collected before you stopped participating. You will be provided a copy of this form.
To be enrolled in the ZYPREXA RELPREVV Patient Care Program, complete and fax this form to 1-877-772-9391.

**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 RELPREVV, Eli Lilly and Company and their delegates run the ZYPREXA RELPREVV Patient Care Program.

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

The ZYPREXA RELPREVV 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 RELPREVV Patient Care Program.
• Your information will be stored in the ZYPREXA RELPREVV Patient Care Program computer system.
• The information will be used to help Lilly learn more about the safety of ZYPREXA RELPREVV.
• Information from all patients in the ZYPREXA RELPREVV 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 RELPREVV 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 RELPREVV Patient Care Program registry to get ZYPREXA RELPREVV.
• I agree to have my information entered in the ZYPREXA RELPREVV Patient Care Program registry.
• My doctor has explained the risks and benefits of treatment with ZYPREXA RELPREVV.
• 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 RELPREVV.
• I may be asked to complete occasional surveys about my understanding of the risks and benefits of treatment with ZYPREXA RELPREVV.
• I or my caregiver have discussed any questions or concerns about my treatment with ZYPREXA RELPREVV with my doctor.

You may stop participating in the ZYPREXA RELPREVV 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 RELPREVV Patient Care Program except to answer safety questions. The ZYPREXA RELPREVV Patient Care Program will still use information that was collected before you stopped participating. You will be provided a copy of this form.

_________________________________________ Date: ____________
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.

_________________________________________ Date: ____________
Signature of Prescriber

Printed Name of Prescriber
Does the patient have a diagnosis of schizophrenia?  

No  
Yes  

**PATIENT/INJECTION INFORMATION**

<table>
<thead>
<tr>
<th>Date of Injection:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>month</td>
<td></td>
</tr>
<tr>
<td>day</td>
<td></td>
</tr>
<tr>
<td>year</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time of ZYPREXA RELPREVV Injection:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>24-hour clock</td>
<td>:</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Interval</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - 15 minutes</td>
<td></td>
</tr>
<tr>
<td>16 - 30 minutes</td>
<td></td>
</tr>
<tr>
<td>31 - 45 minutes</td>
<td></td>
</tr>
<tr>
<td>46 - 60 minutes</td>
<td></td>
</tr>
<tr>
<td>61 - 90 minutes</td>
<td>(1 ½ hours)</td>
</tr>
<tr>
<td>91 - 120 minutes</td>
<td>(2 hours)</td>
</tr>
<tr>
<td>121 - 150 minutes</td>
<td>(2 ½ hours)</td>
</tr>
<tr>
<td>151 - 180 minutes</td>
<td>(3 hours)</td>
</tr>
<tr>
<td>If greater than 3 hours</td>
<td>Please specify:</td>
</tr>
<tr>
<td></td>
<td>Hours</td>
</tr>
</tbody>
</table>

**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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FAX 1-877-772-9391  
www.zyprexarelprevvprogram.com
Patient No.: □ □ □ □ □ □

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 RELPREVV?

□ 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>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Phone 1-877-772-9390  FAX 1-877-772-9391  www.zyprexarelprevvprogram.com
Did the patient receive any NON-PHARMACEUTICAL TREATMENTS or DIAGNOSTIC TESTS associated with this event?  □ Yes - Please record below  □ No

- Assisted ventilation
- EEG
- MRI
- Assisted ventilation
- IV fluids
- Observation/symptomatic management
- Urine drug screen
- MRI
- 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>
</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 Name ______________________ MI ____________________ Last Name ______________________

Title/Occupation: ________________________________________________________

If agent of the Prescriber, name of Prescriber: _________________________________________      _________

__________________________________________________________________________

Phone 1-877-772-9390  FAX 1-877-772-9391  www.zyprexarelprevvprogram.com
# 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)

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 dispense, prior to the vial 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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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 prescriber may be enrolled in the ZYPREXA RELPREVV 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 RELPREVV 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 RELPREVV Patient Care Program requirements and the risks associated with ZYPREXA RELPREVV.

• I have completed the mandatory ZYPREXA RELPREVV 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 RELPREVV.

• I understand that ZYPREXA RELPREVV should only be initiated in patients for whom tolerability with oral olanzapine has been established;

• I understand that ZYPREXA RELPREVV 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 RELPREVV Patient Care Program registry prior to prescribing ZYPREXA RELPREVV by completing the Patient Registration Form.

• I will ensure all suspected cases of PDSS are reported to the ZYPREXA RELPREVV Patient Care Program within 24 hours of becoming aware of the event.

• I will review the ZYPREXA RELPREVV Medication Guide with each patient prior to prescribing.

• I understand that the ZYPREXA RELPREVV 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 RELPREVV 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 RELPREVV.

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

Date: _____/_____/______

Prescriber Signature

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

Version 2.0 03Aug2012  CONFIDENTIAL

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ZYPREXA® RELPREVV™ and the ZYPREXA RELPREVV logo are registered trademarks of Eli Lilly and Company
SINGLE 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 injections. If you are aware that the patient’s prescriber has changed, please notify the ZYPREXA RELPREVV Patient Care Program Coordinating Center.

<table>
<thead>
<tr>
<th>Patient No.:</th>
<th>Injection Facility Name: ________________________________</th>
</tr>
</thead>
<tbody>
<tr>
<td>PIN</td>
<td></td>
</tr>
</tbody>
</table>

Patient Name:

First ____________________________ MI ____________________________ Last ____________________________

Date of Birth: __________-________-________

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: __________-________-________

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: __________-________-________

Healthcare Facility Staff Member Name (print): ________________________________

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

Version 2.0 03Aug2012  CONFIDENTIAL
ZYPREXA® RELPREVV™ is a long-acting atypical antipsychotic for intramuscular injection indicated for the treatment

**DOSAGE AND ADMINISTRATION**

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

ZYPREXA RELPREVV is intended for deep intramuscular gluteal injection only.

- Do not administer intravenously or subcutaneously. (2.1)
- Be aware that there are two ZYPREXA intramuscular formulations with different dosing schedules. ZYPREXA IntraMuscular (10 mg/vial) is a short-acting formulation and should not be confused with ZYPREXA RELPREVV. (2.1)
- Establish tolerability with oral olanzapine prior to initiating treatment. (2.1)
- ZYPREXA RELPREVV doses above 405 mg every 4 weeks or 300 mg every 2 weeks have not been evaluated in clinical trials. (2.1)
- Use in specific populations (including renal and hepatic impaired, and pediatric population) has not been studied. (2.1)
- Must be suspended using only the diluent for ZYPREXA RELPREVV provided in the convenience kit. (2.2)

**DOSE FORMS AND STRENGTHS**

Powder for suspension for intramuscular use only: 210 mg/2 vials, 300 mg/4 vials, and 405 mg/4 vials (3, 11, 16)

ZYPREXA RELPREVV (olanzapine)

**INDICATIONS AND USAGE**

- Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. ZYPREXA RELPREVV is not approved for the treatment of patients with dementia-related psychosis. (5.3, 5.16, 17.3)

**CONTRAINDICATIONS**

None.

**WARNINGS AND PRECAUTIONS**

- 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 should accompany drug therapy. (5.4)
- Neutropenia: Manage with immediate discontinuation and close monitoring. (5.5)

**ADVERSE REACTIONS**

Most common adverse reactions (≥5% in at least one of the treatment groups and greater than placebo) associated with ZYPREXA RELPREVV treatment: headache, sedation, weight gain, cough, diarrhea, back pain, nausea, somnolence, dry mouth, nasopharyngitis, increased appetite, and vomiting. (6.1)

**Full Prescribing Information:**
See full prescribing information for ZYPREXA RELPREVV.

**HIGHLIGHTS OF PRESCRIBING INFORMATION**
See 17 for Patient Counseling Information and FDA-approved Medication Guide

**RECENT MAJOR CHANGES**

None.

**DOSAGE FORMS AND STRENGTHS**

Powder for suspension for intramuscular use only: 210 mg/2 vials, 300 mg/4 vials, and 405 mg/4 vials (3, 11, 16)

**CONTRAINDICATIONS**

None.

**WARNINGS AND PRECAUTIONS**

- 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)

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**Full Prescribing Information:**
See full prescribing information for ZYPREXA RELPREVV.

**HIGHLIGHTS OF PRESCRIBING INFORMATION**
See 17 for Patient Counseling Information and FDA-approved Medication Guide

**RECENT MAJOR CHANGES**

None.

**DOSAGE FORMS AND STRENGTHS**

Powder for suspension for intramuscular use only: 210 mg/2 vials, 300 mg/4 vials, and 405 mg/4 vials (3, 11, 16)

**CONTRAINDICATIONS**

None.

**WARNINGS AND PRECAUTIONS**

- 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)
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**Full Prescribing Information:**
See full prescribing information for ZYPREXA RELPREVV.

**HIGHLIGHTS OF PRESCRIBING INFORMATION**
See 17 for Patient Counseling Information and FDA-approved Medication Guide

**RECENT MAJOR CHANGES**

None.

**DOSAGE FORMS AND STRENGTHS**

Powder for suspension for intramuscular use only: 210 mg/2 vials, 300 mg/4 vials, and 405 mg/4 vials (3, 11, 16)

**CONTRAINDICATIONS**

None.

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**Full Prescribing Information:**
See full prescribing information for ZYPREXA RELPREVV.

**HIGHLIGHTS OF PRESCRIBING INFORMATION**
See 17 for Patient Counseling Information and FDA-approved Medication Guide

**RECENT MAJOR CHANGES**

None.

**DOSAGE FORMS AND STRENGTHS**

Powder for suspension for intramuscular use only: 210 mg/2 vials, 300 mg/4 vials, and 405 mg/4 vials (3, 11, 16)

**CONTRAINDICATIONS**

None.

**WARNINGS AND PRECAUTIONS**

- 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 should accompany drug therapy. (5.4)
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**Full Prescribing Information:**
See full prescribing information for ZYPREXA RELPREVV.

**HIGHLIGHTS OF PRESCRIBING INFORMATION**
See 17 for Patient Counseling Information and FDA-approved Medication Guide

**RECENT MAJOR CHANGES**

None.

**DOSAGE FORMS AND STRENGTHS**

Powder for suspension for intramuscular use only: 210 mg/2 vials, 300 mg/4 vials, and 405 mg/4 vials (3, 11, 16)

**CONTRAINDICATIONS**

None.

**WARNINGS AND PRECAUTIONS**

- 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)
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Most common adverse reactions (≥5% in at least one of the treatment groups and greater than placebo) associated with ZYPREXA RELPREVV treatment: headache, sedation, weight gain, cough, diarrhea, back pain, nausea, somnolence, dry mouth, nasopharyngitis, increased appetite, and vomiting. (6.1)

**Full Prescribing Information:**
See full prescribing information for ZYPREXA RELPREVV.

**HIGHLIGHTS OF PRESCRIBING INFORMATION**
See 17 for Patient Counseling Information and FDA-approved Medication Guide

**RECENT MAJOR CHANGES**

None.

**DOSAGE FORMS AND STRENGTHS**

Powder for suspension for intramuscular use only: 210 mg/2 vials, 300 mg/4 vials, and 405 mg/4 vials (3, 11, 16)

**CONTRAINDICATIONS**

None.

**WARNINGS AND PRECAUTIONS**

- 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 should accompany drug therapy. (5.4)
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**Full Prescribing Information:**
See full prescribing information for ZYPREXA RELPREVV.

**HIGHLIGHTS OF PRESCRIBING INFORMATION**
See 17 for Patient Counseling Information and FDA-approved Medication Guide

**RECENT MAJOR CHANGES**

None.
FULL PRESCRIBING INFORMATION

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

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 [see Dosage and Administration (2.1), Warnings and Precautions (5.1, 5.2), Overdose (10.2), and Patient Counseling Information (17.2)].

Increased Mortality in Elderly Patients with Dementia-Related Psychosis — Elderly patients with dementia-related psychosis treated with atypical antipsychotics are at an increased risk of death. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotics, revealed a risk of death in 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 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 [see Warnings and Precautions (5.5, 5.16) and Patient Counseling Information (17.3)].

INDICATIONS AND USAGE

ZYPREXA RELPREVV is available only through a restricted distribution program [see Warnings and Precautions (5.2)]. ZYPREXA RELPREVV must not be dispensed directly to a patient. For a patient to receive treatment, the prescriber, healthcare facility, patient, and pharmacy must all be enrolled in the ZYPREXA RELPREVV Patient Care Program. To enroll, call 1-877-772-9390.

1. Schizophrenia

ZYPREXA RELPREVV is indicated for the treatment of schizophrenia. Efficacy was established in two clinical trials in patients with schizophrenia: one 8-week trial in adults and one maintenance trial in adults [see Clinical Studies (14.1)].

2. DOSAGE AND ADMINISTRATION

2.1 Dosage

ZYPREXA RELPREVV is intended for deep intramuscular glucose injection only and should not be administered intravenously or subcutaneously.

Be aware that there are two ZYPREXA intramuscular formulations with different dosing schedules. ZYPREXA IntraMuscular (10 mg/vial) is a short-acting formulation and should not be confused with ZYPREXA RELPREVV. Refer to the packaging insert for ZYPREXA IntraMuscular for more information about that product.

Establish tolerability with oral olanzapine prior to initiating treatment.

ZYPREXA RELPREVV should be administered by a healthcare professional every 2 to 4 weeks by deep intramuscular glucose injection using a 19-gauge, 1.5-inch needle. Following insertion of the needle into the muscle, aspiration should be maintained for several seconds to ensure that no blood is drawn into the syringe. If any blood is aspirated into the syringe, it should be discarded and fresh drug should be prepared using a new convenience kit. The injection should be performed at a steady, continuous pressure. Do not massage the injection site.

Dose Selection — The efficacy of ZYPREXA RELPREVV has been demonstrated within the range of 150 mg to 300 mg administered every 2 weeks and with 405 mg administered every 4 weeks. Dose recommendations considering oral ZYPREXA and ZYPREXA RELPREVV are shown in Table 1

Table 1: Recommended Dosing for ZYPREXA RELPREVV Based on Correspondence to Oral ZYPREXA Doses

<table>
<thead>
<tr>
<th>Target Oral ZYPREXA Dose</th>
<th>Dosing of ZYPREXA RELPREVV 8 Weeks During the First 8 Weeks</th>
<th>Maintenance Dose After 8 Weeks ZYPREXA RELPREVV Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mg/day</td>
<td>210 mg/2 weeks or 405 mg/4 weeks</td>
<td>150 mg/2 weeks or 300 mg/4 weeks</td>
</tr>
<tr>
<td>15 mg/day</td>
<td>300 mg/2 weeks</td>
<td>210 mg/2 weeks or 405 mg/4 weeks</td>
</tr>
<tr>
<td>20 mg/day</td>
<td>300 mg/2 weeks</td>
<td>300 mg/2 weeks</td>
</tr>
</tbody>
</table>

ZYPREXA RELPREVV doses greater than 405 mg every 4 weeks or 300 mg every 2 weeks have not been evaluated in clinical trials.

Post-Injection Delirium/Sedation Syndrome — 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 [see Boxed Warning, Warnings and Precautions (5.1), and Overdose (10.1)]. Patients should be informed of this risk and how to recognize related symptoms [see Patient Counseling Information (17.1, 17.2)]. ZYPREXA RELPREVV must be administered in a registered healthcare facility with ready access to emergency response services. After each injection of ZYPREXA RELPREVV injection, a healthcare professional must continuously observe the patient at the healthcare facility for at least 3 hours for symptoms consistent with olanzapine overdose, including sedation (ranging from mild in severity to coma) and/or delirium (including confusion, disorientation, agitation, anxiety, and other cognitive impairment). Other symptoms noted include extrapyramidal symptoms, dysarthria, ataxia, agression, diziness, amnesia, hypotension, and coma. The potential for onset of an 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. Following the 3-hour observation period, healthcare professionals must confirm that the patient is alert, oriented, and absent of any signs and symptoms of post-injection delirium/sedation syndrome prior to being released. All patients must be accompanied to their destination upon leaving the facility. For the remainder of the day of each injection, patients should not drive or operate heavy machinery, and should be advised to be vigilant for symptoms of post-injection delirium/sedation syndrome and be able to obtain medical assistance if needed. If post-injection delirium/sedation syndrome is suspected, close medical supervision and monitoring should be instituted in a facility capable of resuscitation [see Overdose (10.1)].

Dosing in Specific Populations — Tolerance of oral ZYPREXA should be established prior to initiating treatment with ZYPREXA RELPREVV. The recommended starting dose is ZYPREXA RELPREVV 150 mg/4 weeks 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 (5.18), Drug Interactions (7), and Clinical Pharmacology (12.3)]. ZYPREXA RELPREVV has not been studied in subjects under 16 years of age [see Warnings and Precautions (5.7)].

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 of 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 glucose injection only. Not to be injected intravenously or subcutaneously.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Step 1: Preparing Materials

Convenience kit includes:

- Vial of ZYPREXA RELPREVV powder
- 3-mL vial of diluent
- One 3-mL syringe 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 (50 mm), 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 to powder 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>Dose</th>
<th>Vial Strength</th>
<th>Diluent to Add</th>
</tr>
</thead>
<tbody>
<tr>
<td>150 mg</td>
<td>210 mg</td>
<td>1.3 mL</td>
</tr>
<tr>
<td>210 mg</td>
<td>210 mg</td>
<td>1.3 mL</td>
</tr>
<tr>
<td>300 mg</td>
<td>300 mg</td>
<td>1.8 mL</td>
</tr>
<tr>
<td>405 mg</td>
<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 needlestick injury.

Loosen the powder by lightly tapping the vial.

ZYPREXA RELPREVV (olanzapine)

For Extended Release Injectable Suspension

ZYR-0007-USPI-20180119

ZYR-0007-USPI-20180119
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.

FIGURE 1: Tap firmly to mix.

Visually check the vial for clumps. Unsuspended powder appears as yellow, dry clumps clinging to the vial. Additional tapping may be required if large clumps remain (see Figure 2).

FIGURE 2: Check for unsuspended powder and repeat tapping if needed.

Vigorously shake vial.

If foam forms, let vial stand to allow foam to dissipate.

If the product is not used right away, it should be shaken vigorously to re-suspend. Reconstituted ZYPREXA RELPREVV remains stable for up to 24 hours in the vial.

FIGURE 3: Vigorously shake vial.

Step 4: Injecting ZYPREXA RELPREVV

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.

Refer to the table below to determine the final volume to inject. Suspension concentration is 150 mg/mL ZYPREXA RELPREVV.

<table>
<thead>
<tr>
<th>Dose</th>
<th>Final Volume to Inject</th>
</tr>
</thead>
<tbody>
<tr>
<td>150 mg</td>
<td>1 mL</td>
</tr>
<tr>
<td>210 mg</td>
<td>1.4 mL</td>
</tr>
<tr>
<td>300 mg</td>
<td>2 mL</td>
</tr>
<tr>
<td>405 mg</td>
<td>2.7 mL</td>
</tr>
</tbody>
</table>

ZYPREXA RELPREVV (olanzapine)  
For Extended Release Injectable Suspension ZYPR-0007-USPI-20180119

Attach a new safety needle to the syringe.

Slowly withdraw the desired amount into the syringe.

Some excess product will remain in the vial.

Engage the needle safety device and remove needle from syringe.

For administration, select the 19-gauge, 1.5-inch (38 mm) Hypodermic Needle-Pro needle with needle protection device. For obese patients, a 2-inch (50 mm), 19-gauge or larger needle (not included in convenience kit) may be used. To help prevent clogging, a 19-gauge or larger needle must be used.

Attach the new safety needle to the syringe prior to injection. Once the suspension has been removed from the vial, it should be injected immediately.

For deep intramuscular gluteal injection only. Do not inject intravenously or subcutaneously.

Select and prepare a site for injection in the gluteal area. After insertion of the needle into the muscle, aspirate for several seconds to ensure that no blood appears. If any blood is drawn into the syringe, discard the syringe and the dose and begin with a new convenience kit. The injection should be performed with steady, continuous pressure.

Do not massage the injection site.

Engage the needle safety device.

Dispose of the vials, needles, and syringe appropriately after injection. The vial is for single-use only.

3 DOSAGE FORMS AND STRENGTHS

ZYPREXA RELPREVV is a powder for suspension for intramuscular use only. ZYPREXA RELPREVV is present as a yellow solid in a glass vial equivalent to 210, 300, or 405 mg olanzapine per vial. The diluent is a clear, colorless to slightly yellow solution in a glass vial [see Description (11) and How Supplied/Storage and Handling (16)]. The reconstituted suspension will be yellow and opaque [see Dosage and Administration (2.2)].

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Post-Injection Delirium/Sedation Syndrome

During premarketing clinical studies of ZYPREXA RELPREVV, 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 [see Boxed Warning and Dosage and Administration (2.1)]. These events occurred in <0.1% of injections and in approximately 2% of patients who received injections for up to 46 months. These events 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 events, 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, hypertension, 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 Overdosage (10.1)].

Healthcare professionals are advised to discuss this potential risk with patients each time they prescribe and administer ZYPREXA RELPREVV [see Patient Counseling Information (17.1, 17.2)].

5.2 Prescribing and Distribution Program for ZYPREXA RELPREVV

ZYPREXA RELPREVV is available only through a restricted distribution program [see Boxed Warning, Indications and Usage (1), and Patient Counseling Information (17.2)]. ZYPREXA RELPREVV must not be dispensed directly to a patient. For a patient to receive treatment, the prescriber, healthcare facility, patient, and pharmacy must all be enrolled in the ZYPREXA RELPREVV Patient Care Program. To enroll, call 1-877-772-9380. ZYPREXA RELPREVV must be administered in a registered healthcare facility (such as a hospital, clinic, residential treatment center, or community healthcare center) with ready access to emergency response services. After each ZYPREXA RELPREVV injection, a healthcare professional must continuously observe the patient at the healthcare facility for at least 3 hours and must confirm that the patient is alert, oriented, and absent of any signs and symptoms of post-injection delirium/sedation syndrome prior to being released. All patients must be accompanied to their destination upon leaving the facility. For the remainder of the day of each injection, patients should not drive or operate heavy machinery, and should be advised to be vigilant for symptoms of post-injection delirium/sedation syndrome and be able to obtain medical assistance if needed. 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)]. If parenteral benzodiazepines are required for patient management during an event of post-injection delirium/sedation syndrome, careful evaluation of clinical status for excessive sedation and cardiopulmonary depression is recommended.

5.3 Elderly Patients with Dementia-Related Psychosis

Increased Mortality

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. ZYPREXA RELPREVV is not approved for the treatment of patients with dementia-related psychosis [see Boxed Warning, Warnings and Precautions (5.16), and Patient Counseling Information (17.3)].

ZYPREXA RELPREVV (olanzapine)  
For Extended Release Injectable Suspension ZYPR-0007-USPI-20180119

ZYPREXA RELPREVV (olanzapine)  
For Extended Release Injectable Suspension ZYPR-0007-USPI-20180119

Zyproxa Relprev, ZYPR-0007-USPI-20180119_ZYPR-0001-MG-20161006

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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 (3.3% vs 1.5%, respectively).

Cerebrovascular or Adverse Events (CVAE), including:

Cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, 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. ZYPREXA Relprevir is not approved for the treatment of patients with dementia-related psychosis (see Boxed Warning and Patient Counseling Information [17.2]).

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 Neuroleptic Malignant Malignant Syndrome (NMS)

A potentially fatal symptom complex sometimes referred to as Neuroleptic 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 (irregular pulse or blood pressure, tachycardia, diaphoresis and cardiac dysrhythmia). Additional signs may include elevated creatinine 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 untreated 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 treatment regimens are available. There is no general agreement about specific pharmacological treatment regimens for NMS.

If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered and tolerability with oral olanzapine should be established prior to initiation of treatment with ZYPREXA Relprevir (see Dosage and Administration [2.1]). The patient should be carefully monitored, since recurrences of NMS have been reported (see Patient Counseling Information [17.4]).

5.6 Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) has been reported with olanzapine exposure. DRESS may present with a cutaneous reaction (such as rash or exfoliative dermatitis), eosinophilia, fever, and/or lymphadenopathy with systemic complications including hepatitis, nephritis, pneumonitis, myositis, and/or pericarditis. DRESS is sometimes fatal. Discontinue ZYPREXA Relprevir if DRESS is suspected (see Patient Counseling Information [17.5]).

5.7 Metabolic Changes

Atypical antipsychotic drugs have been associated with metabolic changes including hyperglycemia, dyslipidemia, and weight gain. Metabolic changes may be associated with increased cardiovascular/cerebrovascular risk. Olanzapine’s specific metabolic profile is presented below.

Hyperglycemia and Diabetes Mellitus

Physicians should consider the risks and benefits when prescribing olanzapine to patients with an established diagnosis of diabetes mellitus, or having borderline increased blood 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 an atypical antipsychotic drug should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug (see Patient Counseling Information [17.6]).

Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics including olanzapine. Assessment of the relationship between atypical 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. Epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related adverse reactions in patients treated with the atypical antipsychotics. While relative risk estimates are consistent, the association between atypical antipsychotics and increases in glucose levels appears to fall on a continuum and olanzapine appears to have a greater association than some other atypical antipsychotics.

Mean increases in blood glucose have been observed in patients treated (median exposure of 9.2 months) with olanzapine in phase 1 of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE). 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 compared to baseline in fasting blood glucose of 2.3 mg/dL. Placebo-treated subjects (N=19) had a mean increase in fasting blood glucose compared to baseline of 0.34 mg/dL.

Olanzapine Monotherapy in Adults — In an analysis of 5 placebo-controlled adult olanzapine monotherapy studies with a median treatment duration of approximately 3 weeks, olanzapine was associated with a greater mean change in fasting glucose levels compared to placebo (2.76 mg/dL versus 0.17 mg/dL). The difference in mean changes between olanzapine and placebo was greater in patients with evidence of glucose dysregulation at baseline (patients diagnosed with diabetes mellitus or related adverse reactions, patients treated with anti-diabetic agents, patients with a baseline random glucose level >200 mg/dL, and/or a baseline fasting glucose level >126 mg/dL).

Olanzapine-treated patients had a greater mean HbA1c, increase from baseline of 0.04% (median exposure 21 days), compared to a mean HbA1c decrease of 0.06% in placebo-treated subjects (median exposure 17 days).

In an analysis of 8 placebo-controlled studies (median treatment exposure 4-5 weeks), 6.1% of olanzapine-treated subjects (N=855) had treatment-emergent glycosuria compared to 2.8% of placebo-treated subjects (N=599). Table 2 shows short-term and long-term changes in fasting glucose levels from adult olanzapine monotherapy studies.

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>N</th>
<th>Patients</th>
<th>N</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Glucose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal to High</td>
<td>(&lt;100 mg/dL to ≥126 mg/dL)</td>
<td>Olanzapine</td>
<td>543</td>
<td>2.2%</td>
<td>345</td>
<td>12.8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo</td>
<td>293</td>
<td>3.4%</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Borderline to High</td>
<td>(≥100 mg/dL and &lt;126 mg/dL to ≥126 mg/dL)</td>
<td>Olanzapine</td>
<td>178</td>
<td>17.4%</td>
<td>127</td>
<td>26.0%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo</td>
<td>96</td>
<td>11.5%</td>
<td>NA</td>
<td>NA</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 patients who completed <12 months of olanzapine therapy, mean change in fasting and nonfasting glucose levels continued to increase over time.

Olanzapine Monotherapy in Adolescents — The safety and efficacy of ZYPREXA Relprevir 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>N</th>
<th>Patients</th>
<th>N</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Glucose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal to High</td>
<td>(&lt;100 mg/dL to ≥126 mg/dL)</td>
<td>Olanzapine</td>
<td>124</td>
<td>0.9%</td>
<td>108</td>
<td>0.9%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo</td>
<td>53</td>
<td>1.9%</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Borderline to High</td>
<td>(≥100 mg/dL and &lt;126 mg/dL to ≥126 mg/dL)</td>
<td>Olanzapine</td>
<td>14</td>
<td>14.3%</td>
<td>13</td>
<td>23.1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo</td>
<td>13</td>
<td>0.0%</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

* Not Applicable.

Dyslipidemia

Undesirable alterations in lipids have been observed with olanzapine use. Clinical monitoring, including baseline and periodic follow-up lipid evaluations in patients using olanzapine, is recommended (see Patient Counseling Information [17.7]).

Clinically significant, and sometimes very high (>500 mg/dL), elevations in triglyceride levels have been observed with olanzapine use. Modest mean increases in total cholesterol have also been seen with olanzapine use.

Olanzapine Monotherapy in Adults — In an analysis of 5 placebo-controlled olanzapine monotherapy studies with treatment duration up to 12 weeks, olanzapine-treated patients had increases from baseline in mean fasting total cholesterol, LDL cholesterol, and triglycerides of 5.3 mg/dL, 3.0 mg/dL, and 20.8 mg/dL respectively compared to decreases from baseline in mean fasting total cholesterol, LDL cholesterol, and triglycerides of 6.1 mg/dL, 4.3 mg/dL, and 10.7 mg/dL for placebo-treated patients. For fasting HDL cholesterol, no clinically meaningful differences were observed between olanzapine-treated patients and placebo-treated patients.

Mean increases in fasting lipid values (total cholesterol, LDL cholesterol, and triglycerides) were greater in patients without evidence of lipid dysregulation at baseline, where lipid dysregulation was defined as patients diagnosed with dyslipidemia or related adverse reactions, patients treated with lipid lowering agents, or patients with high baseline lipid levels.
In long-term studies (at least 48 weeks), patients had increases from baseline in mean fasting total cholesterol, LDL cholesterol, and triglycerides of 5.6 mg/dL, 2.5 mg/dL, and 18.7 mg/dL, respectively, and a mean decrease in fasting HDL cholesterol of 0.16 mg/dL. In an analysis of patients who completed 12 months of therapy, the mean nonfasting total cholesterol did not increase further after approximately 4-6 months.

The proportion of patients who had changes (at least once) in total cholesterol, LDL cholesterol or triglycerides from normal or borderline to high, or changes in HDL cholesterol did not increase further after approximately 4-6 months.

In an analysis of patients who completed 12 months of therapy, the mean nonfasting total and LDL cholesterol, and triglycerides increased from baseline in 15.3%, 18.7 mg/dL, and 32.4%, respectively, and a mean decrease in fasting HDL cholesterol of 0.16 mg/dL.

In phase 1 of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE), over a median exposure of 9.4 mg/dL, 12 weeks of exposure was observed. In a 24-week randomized, double-blind, fixed-dose study with ZYPREXA RELPREV, statistically significant differences among dose groups have been observed for fasting triglycerides. Incidence of changes from normal to high levels of fasting triglycerides have been observed in all dose groups. Discontinuation due to weight gain occurred in 0.2% of placebo-treated patients

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

<table>
<thead>
<tr>
<th>Category Change from Baseline</th>
<th>Treatment Arm</th>
<th>Up to 12 weeks exposure</th>
<th>At least 48 weeks exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fasting Triglycerides</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increase by ≥50 mg/dL</td>
<td>Olanzapine 745</td>
<td>39.6% 487</td>
<td>61.4%</td>
</tr>
<tr>
<td>Normal to High (&lt;150 mg/dL to ≥200 mg/dL)</td>
<td>Olanzapine 457</td>
<td>9.2% 293</td>
<td>32.4%</td>
</tr>
<tr>
<td>Borderline to High (≥150 mg/dL and &lt;200 mg/dL to ≥200 mg/dL)</td>
<td>Olanzapine 135</td>
<td>39.3% 75</td>
<td>70.7%</td>
</tr>
<tr>
<td><strong>Fasting Total Cholesterol</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increase by ≥40 mg/dL</td>
<td>Olanzapine 745</td>
<td>21.6% 489</td>
<td>32.9%</td>
</tr>
<tr>
<td>Normal to High (&lt;200 mg/dL to ≥240 mg/dL)</td>
<td>Olanzapine 392</td>
<td>2.8% 283</td>
<td>14.8%</td>
</tr>
<tr>
<td>Borderline to High (≥200 mg/dL and &lt;240 mg/dL to ≥240 mg/dL)</td>
<td>Olanzapine 222</td>
<td>23.0% 125</td>
<td>55.2%</td>
</tr>
<tr>
<td><strong>Fasting LDL Cholesterol</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increase by ≥30 mg/dL</td>
<td>Olanzapine 536</td>
<td>23.7% 483</td>
<td>39.8%</td>
</tr>
<tr>
<td>Normal to High (&lt;100 mg/dL to ≥160 mg/dL)</td>
<td>Olanzapine 154</td>
<td>0% 123</td>
<td>7.3%</td>
</tr>
<tr>
<td>Borderline to High (≥100 mg/dL and &lt;160 mg/dL to ≥160 mg/dL)</td>
<td>Olanzapine 302</td>
<td>10.6% 284</td>
<td>31.0%</td>
</tr>
</tbody>
</table>

*NA Not Applicable.*

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

<table>
<thead>
<tr>
<th>Category Change 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><strong>Fasting Triglycerides</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increase by ≥50 mg/dL</td>
<td>Olanzapine 138</td>
<td>37.0% 122</td>
<td>45.9%</td>
</tr>
<tr>
<td>Normal to High (&lt;90 mg/dL to ≥130 mg/dL)</td>
<td>Olanzapine 67</td>
<td>26.9% 66</td>
<td>36.4%</td>
</tr>
<tr>
<td>Borderline to High (≥90 mg/dL and &lt;130 mg/dL to ≥130 mg/dL)</td>
<td>Olanzapine 37</td>
<td>59.5% 31</td>
<td>64.5%</td>
</tr>
</tbody>
</table>

*NA Not Applicable.*

### Table 6: Changes in Fasting Lipids Values from Adult Olanzapine Monotherapy Studies

<table>
<thead>
<tr>
<th>Category Change 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><strong>Fasting Total Cholesterol</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increase by ≥40 mg/dL</td>
<td>Olanzapine 138</td>
<td>14.5% 122</td>
<td>14.8%</td>
</tr>
<tr>
<td>Normal to High (&lt;170 mg/dL to ≥200 mg/dL)</td>
<td>Olanzapine 87</td>
<td>6.9% 78</td>
<td>7.7%</td>
</tr>
<tr>
<td>Borderline to High (≥170 mg/dL and &lt;200 mg/dL to ≥200 mg/dL)</td>
<td>Olanzapine 36</td>
<td>38.9% 33</td>
<td>57.6%</td>
</tr>
<tr>
<td><strong>Fasting LDL Cholesterol</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increase by ≥30 mg/dL</td>
<td>Olanzapine 137</td>
<td>17.5% 121</td>
<td>22.3%</td>
</tr>
<tr>
<td>Normal to High (&lt;110 mg/dL to ≥130 mg/dL)</td>
<td>Olanzapine 98</td>
<td>5.1% 92</td>
<td>10.9%</td>
</tr>
<tr>
<td>Borderline to High (≥110 mg/dL and &lt;130 mg/dL to ≥130 mg/dL)</td>
<td>Olanzapine 29</td>
<td>48.3% 21</td>
<td>47.6%</td>
</tr>
</tbody>
</table>

*NA Not Applicable.*

### Weight Gain

Potential consequences of weight gain should be considered prior to starting olanzapine. Patients receiving olanzapine should receive regular monitoring of weight (see Patient Counseling Information (17.8)).

**Olanzapine Monotherapy in Adults** — In an analysis of 13 placebo-controlled olanzapine monotherapy studies, olanzapine-treated patients gained an average of 2.6 kg (5.7 lb) compared to a baseline weight loss in placebo-treated patients with a median exposure of 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 in 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 exposure of 573 days, N = 2021). The percentages of patients who gained at least 7%, 15%, or 25% of their baseline body weight with long-term exposure were 64%, 32%, and 12%, 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 Olanzapine Use in Adults

<table>
<thead>
<tr>
<th>Amount Gained kg (lb)</th>
<th>6 Weeks (N=7465) (%)</th>
<th>6 Months (N=3162) (%)</th>
<th>12 Months (N=1535) (%)</th>
<th>24 Months (N=747) (%)</th>
<th>36 Months (N=147) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤0</td>
<td>26.2 24.3 20.8</td>
<td>23.2 17.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 to &lt;5 (0-11 lb)</td>
<td>57.0 36.0 26.0</td>
<td>23.4 25.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥5 to ≤10 (11-22 lb)</td>
<td>14.9 24.6 24.2</td>
<td>24.1 18.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥10 to ≤15 (22-33 lb)</td>
<td>1.8 10.9 14.9</td>
<td>11.4 17.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥15 to ≤20 (33-44 lb)</td>
<td>0.1 3.1 8.6</td>
<td>9.3 11.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;20 to ≤25 (44-55 lb)</td>
<td>0 0.9 3.3</td>
<td>5.1 4.1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;25 to ≤30 (55-66 lb)</td>
<td>0 0.2 1.4</td>
<td>2.3 4.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;30 (≥66 lb)</td>
<td>0 0.1 0.8</td>
<td>1.2 2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*NA Not Applicable.*
Dose group differences with respect to weight gain have been observed in some studies. In a 24-week randomized, double-blind, fixed-dose study with ZYPREXA RELPREVV, mean baseline-to-endpoint increase in weight (150 mg/2 weeks, n=142; 0.67 kg; 405 mg/4 weeks, n=315; 0.99 kg; 300 mg/2 weeks, n=140; 1.70 kg) was observed with significant differences between the lowest and highest dose groups (150 mg vs 300 mg/2 weeks). 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 adult patients with schizophrenia or schizoaffective disorder, mean baseline to endpoint increase in weight (10 mg/day: 1.9 kg; 20 mg/day: 2.3 kg; 40 mg/day: 3 kg) was observed with significant differences between 10 vs 40 mg/day.

Olanzapine Monotherapy in Adolescents — The safety and efficacy of ZYPREXA RELPREVV have not been established in patients under the age of 18 years. Mean increase in weight in adolescents was greater than in adults. In 4 placebo-controlled trials, discontinuation due to weight gain occurred in 1% of olanzapine-treated patients, compared to 0% of placebo-treated patients.

<table>
<thead>
<tr>
<th>Amount Gained (kg)</th>
<th>6 Weeks (N=243) (%)</th>
<th>6 Months (N=191) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤0</td>
<td>2.9</td>
<td>2.1</td>
</tr>
<tr>
<td>0 to ≤5 (0-11 lb)</td>
<td>47.3</td>
<td>24.6</td>
</tr>
<tr>
<td>&gt;5 to ≤10 (11-22 lb)</td>
<td>42.4</td>
<td>26.7</td>
</tr>
<tr>
<td>&gt;10 to ≤15 (22-33 lb)</td>
<td>5.8</td>
<td>22.0</td>
</tr>
<tr>
<td>&gt;15 to ≤20 (33-44 lb)</td>
<td>0.8</td>
<td>12.6</td>
</tr>
<tr>
<td>&gt;20 to ≤25 (44-55 lb)</td>
<td>0.8</td>
<td>9.4</td>
</tr>
<tr>
<td>&gt;25 to ≤30 (55-66 lb)</td>
<td>0</td>
<td>2.1</td>
</tr>
<tr>
<td>&gt;30 to ≤35 (66-77 lb)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>&gt;35 to ≤40 (77-88 lb)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>&gt;40 (≥88 lb)</td>
<td>0</td>
<td>0.5</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Olanzapine-treated patients</th>
<th>Placebo-treated patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean change in body weight from baseline (median exposure = 3 weeks)</td>
<td>4.6 kg (10.1 lb)</td>
</tr>
<tr>
<td>Percentage of patients who gained at least 7% of baseline body weight</td>
<td>40.6% (median exposure to 7% = 4 weeks)</td>
</tr>
<tr>
<td>Percentage of patients who gained at least 15% of baseline body weight</td>
<td>7.1% (median exposure to 15% = 19 weeks)</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 baseline BMI category was 11.5 kg (25.3 lb), 12.1 kg (26.6 lb), and 12.7 kg (27.9 lb), respectively, for normal (N=106), overweight (N=26) 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

Given these considerations, olanzapine should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic antipsychotic treatment 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.

### 5.9 Orthostatic Hypotension

ZYPREXA RELPREVV may induce orthostatic hypotension associated with dizziness, tachycardia, bradycardia and, in some patients, syncope, probably reflecting its α-2 adrenergic antagonistic properties [see Patient Counseling Information (17.9)]. Syncope-related adverse reactions were reported in 0.1% of patients treated with ZYPREXA RELPREVV in clinical studies. From an analysis of the vital sign data in an integrated database of 41 completed clinical studies in adult patients treated with oral olanzapine, orthostatic hypotension was recorded in ≥20% (1277/6030) of patients.

Olanzapine should be used with particular caution in patients with known cardiovascular disease (history of myocardial infarction or ischemia, heart failure, or conduction abnormalities), cerebrovascular disease, and conditions which would predispose patients to hypotension (dehydration, hypovolemia, and treatment with antihypertensive medications) where the occurrence of syncope, or hypotension and/or bradycardia might put the patient at increased medical risk. For patients in this population who have never taken olanzapine, tolerability 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 hypotension, bradycardia, respiratory or central nervous system depression [see Drug Interactions (7)].

### 5.10 Falls

ZYPREXA RELPREVV may cause somnolence, postural hypotension, motor and sensory instability, which may lead to falls and, consequently, fractures or other injuries. For patients with diseases, conditions, or medications that could exacerbate these effects, complete fall risk assessments when initiating antipsychotic treatment and recurrently for patients on long-term antipsychotic therapy.

### 5.11 Leukopenia, Neutropenia, and Agranulocytosis

In clinical trial and/or postmarketing experience, events of leukopenia/neutropenia have been 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/neutrophilia should have their complete blood count (CBC) monitored frequently during the first few months of therapy and discontinuation of ZYPREXA RELPREVV should be considered at the first sign of a clinically significant decline in WBC in the absence of other causative factors. Patients with clinically significant neutropenia should be carefully monitored for fever or other symptoms or signs of infection and treated promptly if such symptoms or signs occur. Patients with severe neutropenia (absolute neutrophil count <1000/mm³) should discontinue ZYPREXA RELPREVV and have their WBC followed until recovery.

### 5.12 Dysphagia

Esophageal dysmotility and aspiration have been associated with antipsychotic drug use. Aspiration pneumonia is a common 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

During premarketing testing of ZYPREXA RELPREVV, seizures occurred in 0.15% of patients. During premarketing testing of oral olanzapine, seizures occurred in 0.9% of olanzapine-treated patients. There were confounding factors that may have contributed to the occurrence of seizures in many of these cases.

Olanzapine should be used cautiously in patients with a history of seizures or with conditions that potentially lower the seizure threshold, e.g., Alzheimer’s dementia. Olanzapine is not approved for the treatment of patients with Alzheimer’s disease. Conditions that lower the seizure threshold may be more prevalent in a population of 65 years or older.

### 5.14 Potential for Cognitive and Motor Impairment

Sedation was a commonly reported adverse reaction associated with ZYPREXA RELPREVV treatment, occurring at an incidence of 6% 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 premarketing 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 after each injection, 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 (5.4), and Patient Counseling Information (17.10).

### 5.15 Body Temperature Regulation

Disruption of the body’s ability to reduce core body temperature has been attributed to antipsychotic agents. Appropriate care is advised when prescribing ZYPREXA RELPREVV for patients who will be experiencing conditions which may contribute to an elevation in core body temperature, e.g., exercising strenuously, exposure to extreme heat, receiving concomitant

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medication with anticholinergic activity, or being subject to dehydration [see Patient Counseling Information (17.11)].

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)].

Olanzapine exhibits in vitro muscarinic receptor affinity. In premarketing clinical trials with oral olanzapine, olanzapine was associated with constipation, dry mouth, and tachycardia, all adverse reactions possibly related to cholinergic antagonism. Such adverse reactions were not often the basis for discontinuations from olanzapine, but olanzapine should be used with caution in patients with clinically significant prostatic hyper trophy, narrow angle glaucoma, or a history of paralytic ileus or related conditions.

In 5 placebo-controlled studies of oral olanzapine in elderly patients with dementia-related psychosis (n=1184), the following treatment-emergent adverse reactions were reported in olanzapine-treated patients at an incidence of at least 2% and significantly greater than placebo-treated patients: falls, somnolence, peripheral edema, abnormal gait, urinary incontinence, increased weight, asthma, pyrexia, pneumonia, dry mouth and visual hallucinations. The rate of discontinuation due to adverse reactions was significantly greater with oral olanzapine than placebo (13% vs 7%). Elderly patients with dementia-related psychosis treated with olanzapine are at an increased risk of death compared to placebo. Olanzapine is not approved for the treatment of patients with dementia-related psychosis [see Boxed Warning, Warnings and Precautions (5.3), and Patient Counseling Information (17.3)].

Olanzapine has not been evaluated or used to any appreciable extent in patients with a recent history of myocardial infarction or unstable heart disease. Patients with these diagnoses were excluded from premarketing clinical studies. Because of the risk of orthostatic hypotension with olanzapine, caution should be observed in cardiac patients [see Warnings and Precautions (5.9)].

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 steroidogenesis in both female and male patients. Galactorrhea, amenorrhea, gynecomastia, and impotence have been reported in patients receiving prolactin-elevating compounds. Long-standing hyperprolactinemia when associated with hypogonadism may lead to decreased bone density in both female and male subjects.

Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin dependent in vitro, a factor of potential importance if the prescription of these drugs is contemplated in a patient with previously detected breast cancer. As is common with compounds which increase prolactin release, an increase in mammary gland neoplasia was observed in the oral olanzapine carcinogenicity studies conducted in mice and rats [see Nonclinical Toxicology (13.1)]. Neither clinical studies nor epidemiologic studies conducted to date have shown an association between chronic administration of this class of drugs and tumorigenesis in humans; the available evidence is considered too limited to be conclusive at this time.

In placebo-controlled olanzapine clinical studies (up to 12 weeks), changes from normal to high in prolactin concentrations were observed in 30% of adults treated with olanzapine as compared to 10.5% of adults treated with placebo. In a pooled analysis from clinical studies including 8136 adults treated with olanzapine, potentially associated clinical manifestations included menstrual-related events1 (2% [95/8136] of females and males), sexual function-related events2 (2% [150/8136] of females and males), and breast-related events2 (0.7% [23/3240] of females, 0.2% [9/4896] of males).

In placebo-controlled olanzapine monotherapy studies in adolescent patients (up to 6 weeks) with schizophrenia or bipolar I disorder (manic or mixed episodes), changes from normal to high in prolactin concentrations were observed in 47% of olanzapine-treated patients compared to 7% of placebo-treated patients. In a pooled analysis from clinical trials including 454 adolescents treated with olanzapine, potentially associated clinical manifestations included menstrual-related events1 (1% [2/168] of females), sexual function-related events2 (0.7% [3/454] of females and males), and breast-related events2 (2% [3/168] of females, 2% [7/286] of males) [see Use in Specific Populations (8.4)].

1 Based on a search of the following terms: breast discharge, enlargement or swelling, galactorrhea, gynecomastia, and lactation disorder.

2 Based on a search of the following terms: anorgasmia, delayed ejaculation, erectile dysfunction, decreased libido, loss of libido, abnormal orgasm, and sexual dysfunction.

3 Based on a search of the following terms: breast discharge, enlargement or swelling, galactorrhea, gynecomastia, and lactation disorder.

Dose group differences with respect to prolactin elevation have been observed in some studies. In a 24-week randomized, double-blind, fixed-dose study with ZYPREXA RELPREVV, statistically significant differences among dose groups were observed for prolactin levels, with a mean baseline-to-end of study change in the highest dose group (405 mg/2 weeks, n=115: 3.57 mg/mL) relative to mean decreases in the lower dose groups (150 mg/2 weeks, n=109: -5.61 mg/mL; 405 mg/4 weeks, n=259: -2.76 mg/mL). 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 adult patients with schizophrenia or schizoaffective disorder, incidence of prolactin elevation >24.2 ng/mL (female) or >18.77 ng/mL (male) at any time during the trial (10 mg/day: 31.2%; 20 mg/day: 42.7%; 40 mg/day: 61.1%) indicated significant differences between 10 vs 40 mg/day and 20 vs 40 mg/day.

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 (5.7) and Patient Counseling Information (17.6, 17.7)].

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6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

The information below for ZYPREXA RELPREVV is derived primarily from a clinical trial database consisting of 2038 patients with approximately 1948 patient years of exposure to ZYPREXA RELPREVV. This database includes safety data from 6 open-label studies and 2 double-blind comparator studies, conducted in patients with schizophrenia or schizoaffective disorder. Additionally, data obtained from patients treated with oral olanzapine are also presented. Adverse reactions were assessed by the collection of adverse reactions, vital signs, weights, laboratory analyses, ECGs, and the results of physical and ophthalmologic examinations. In the tables and tabulations that follow for ZYPREXA RELPREVV, the MedDRA terminology has been used to classify adverse reactions. Data obtained from oral olanzapine studies was reported using the COSTART and MedDRA dictionaries.

The stated frequencies of adverse reactions represent the proportion of individuals who experienced, at least once, a treatment-emergent adverse reaction of the type listed. A reaction was considered treatment emergent if it occurred for the first time or worsened while receiving therapy following baseline evaluation. Reactions listed elsewhere in labeling may not be repeated below. The entire label should be read to gain a complete understanding of the safety profile of ZYPREXA RELPREVV.

The prescriber should be aware that the figures in the tables and tabulations cannot be used to predict the incidence of side effects in the course of usual medical practice where patient characteristics and other factors differ from those that prevailed in the clinical trials. Similarly, the cited frequencies cannot be compared with figures obtained from other clinical investigations involving different treatments, uses, and investigators. The cited figures, however, do provide the prescribing physician with some basis for estimating the relative contribution of drug and nondrug factors to the adverse reaction incidence in the population studied.

Adverse Reactions Associated with Discontinuation of Treatment in a Short-Term, Placebo-Controlled Trial

Overall, there was no difference in the incidence of discontinuation due to adverse reactions between ZYPREXA RELPREVV (4%; 13/306 patients) and placebo (5%; 5/98) in an 8-week trial.

Commonly Observed Adverse Reactions in a Short-Term, Placebo-Controlled Trial

In an 8-week trial, treatment-emergent adverse reactions with an incidence of 5% or more in at least one of the ZYPREXA RELPREVV treatment groups (210 mg/2 weeks, 405 mg/4 weeks, or 500 mg/2 weeks) and greater than placebo were: headache, sedation, weight gain, cough, diarrhea, back pain, nausea, somnolence, dry mouth, nasopharyngitis, increased appetite, and vomiting.

Adverse Reactions Occurring at an Incidence of 2% or More among ZYPREXA RELPREVV-Treated Patients in a Short-Term, Placebo-Controlled Trial

Table 9 enumerates the incidence, rounded to the nearest percent, of treatment-emergent adverse reactions that occurred in 2% or more of patients treated with ZYPREXA RELPREVV and with incidence greater than placebo who participated in the 8-week, placebo-controlled trial.

Table 9: Treatment-Emergent Adverse Reactions: Incidence in a Short-Term, Placebo-Controlled Clinical Trial with ZYPREXA RELPREVV

<table>
<thead>
<tr>
<th>Body System/Adverse Reaction</th>
<th>Placebo (N=98)</th>
<th>ZYPREXA RELPREVV 405 mg/4 wks (N=100)</th>
<th>ZYPREXA RELPREVV 210 mg/2 wks (N=100)</th>
<th>ZYPREXA RELPREVV 300 mg/2 wks (N=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ear and Labyrinth Disorders</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ear pain</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td><strong>Gastrointestinal Disorders</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4</td>
<td>2</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>1</td>
<td>2</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Flatulence</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Nausea</td>
<td>2</td>
<td>5</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Toothache</td>
<td>0</td>
<td>3</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2</td>
<td>6</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>General Disorders and Administration Site Conditions</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>3</td>
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<tr>
<td>Injection site pain</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Pain</td>
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<td>Pyrexia</td>
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<td><strong>Infections and Infestations</strong></td>
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<td>Nasopharyngitis</td>
<td>3</td>
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<td>Tooth infection</td>
<td>0</td>
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<tr>
<td>Upper respiratory tract infection</td>
<td>2</td>
<td>3</td>
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<td>4</td>
</tr>
<tr>
<td>Viral infection</td>
<td>0</td>
<td>0</td>
<td>0</td>
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</tr>
</tbody>
</table>

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Table 9: Treatment-Emergent Adverse Reactions: Incidence in a Short-Term, Placebo-Controlled Clinical Trial with ZYPREXA RELPREVV (Cont.)

<table>
<thead>
<tr>
<th>Body System/Adverse Reaction</th>
<th>Placebo (N=98)</th>
<th>ZYPREXA RELPREVV 405 mg/4 wks (N=100)</th>
<th>ZYPREXA RELPREVV 210 mg/2 wks (N=106)</th>
<th>ZYPREXA RELPREVV 300 mg/2 wks (N=100)</th>
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</thead>
<tbody>
<tr>
<td>Injury, Poisoning and Procedural Complications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Procedural pain</td>
<td>0</td>
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</tr>
<tr>
<td>Investigations</td>
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<td>Electrocardiogram QT-corrected interval prolonged</td>
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<td>0</td>
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<td>2</td>
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<tr>
<td>Hepatic enzyme increased^</td>
<td>1</td>
<td>4</td>
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<tr>
<td>Weight increased</td>
<td>5</td>
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<td>6</td>
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<tr>
<td>Metabolism and Nutrition Disorders</td>
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<tr>
<td>Increased appetite</td>
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<td>4</td>
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<tr>
<td>Musculoskeletal and Connective</td>
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<td>Arthralgia</td>
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<td>Back pain</td>
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<td>Muscle spasms</td>
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<td>Musculoskeletal stiffness</td>
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<td>Nervous System Disorders</td>
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<td>Dizziness</td>
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<td>Dystarhia</td>
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<td>Headache^</td>
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<tr>
<td>Sedation^</td>
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<td>Tremor</td>
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<td>Psychiatric Disorders</td>
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<td>Abnormal dreams</td>
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<td>Hallucination, auditory</td>
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<td>Restlessness</td>
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<td>Sleep disorder</td>
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<td>Reproductive System and Breast Disorders</td>
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<td>Vaginal discharge</td>
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<tr>
<td>Respiratory, Thoracic and Mediastinal Disorders</td>
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<tr>
<td>Cough</td>
<td>5</td>
<td>3</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Nasal congestion^</td>
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<td>7</td>
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<td>Pharyngolaryngeal pain</td>
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<td>Sneezing</td>
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<td>0</td>
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<td>Skin and Subcutaneous Tissue Disorders</td>
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<td></td>
</tr>
<tr>
<td>Acne</td>
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<td>Vascular Disorders</td>
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</tr>
<tr>
<td>Hypertension</td>
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<tr>
<td>^ The term abdominal pain was upper was combined under abdominal pain.</td>
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<tr>
<td>^ The term tooth abscess was combined under tooth infection.</td>
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</tr>
<tr>
<td>^ The term alanine aminotransferase increased, aspartate aminotransferase increased, and gamma-glutamyltransferase increased were combined under hepatic enzyme increased.</td>
<td></td>
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<tr>
<td>^ The term tension headache was combined under headache.</td>
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<tr>
<td>^ The term somnolence was combined under sedation.</td>
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<tr>
<td>^ The term sinus congestion was combined under nasal congestion.</td>
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<td></td>
</tr>
</tbody>
</table>

Dose Dependency of Adverse Reactions

Dose group differences have been observed for weight, fasting triglycerides and prolactin elevation for ZYPREXA RELPREVV [see Warnings and Precautions (5.7, 5.17)].

A dose group difference for oral olanzapine has been observed for fatigue, dizziness, weight gain and prolactin elevation. 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 adult patients with schizophrenia or schizoaffective disorder, incidence of fatigue (10 mg/day: 1.5%; 20 mg/day: 2.1%; 40 mg/day: 6.6%) was observed with significant differences between 10 vs 40 mg and 20 vs 40 mg/day. The incidence of dizziness (10 mg/day: 2.6%; 20 mg/day: 1.6%; 40 mg/day: 6.6%) was observed with significant differences between 20 mg vs 40 mg. Dose group differences were also noted for weight gain and prolactin elevation [see Warnings and Precautions (5.7, 5.17)].

Table 10: Extrapyramidal Symptoms

Assessed by Rating Scales Incidence in a Fixed Dosage Range, Placebo-Controlled Clinical Trial of Oral Olanzapine in Schizophrenia — Acute Phase

<table>
<thead>
<tr>
<th>Percentage of Patients Reporting Event</th>
<th>Placebo (N=68)</th>
<th>Olanzapine 5 ± 2.5 mg/day (N=65)</th>
<th>Olanzapine 10 ± 2.5 mg/day (N=64)</th>
<th>Olanzapine 15 ± 2.5 mg/day (N=69)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parkinsonism^</td>
<td>15</td>
<td>14</td>
<td>12</td>
<td>27</td>
</tr>
<tr>
<td>Akathisia^</td>
<td>23</td>
<td>16</td>
<td>19</td>
<td>27</td>
</tr>
</tbody>
</table>

^ Percentage of patients with a Simpson-Angus Scale total score <3.

The following table enumerates the percentage of patients with treatment-emergent extrapyramidal symptoms as assessed by spontaneously reported adverse reactions during acute therapy in the same controlled clinical trial comparing olanzapine at 3 fixed doses with placebo in the treatment of schizophrenia in a 6-week trial.

Table 11: Extrapyramidal Symptoms

Assessed by Adverse Reactions Incidence in a Fixed Dosage Range, Placebo-Controlled Clinical Trial of Oral Olanzapine in Schizophrenia — Acute Phase

<table>
<thead>
<tr>
<th>Percentage of Patients Reporting Event</th>
<th>Placebo (N=68)</th>
<th>Olanzapine 5 ± 2.5 mg/day (N=65)</th>
<th>Olanzapine 10 ± 2.5 mg/day (N=64)</th>
<th>Olanzapine 15 ± 2.5 mg/day (N=69)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dys tonic events^</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Parkinsonism events^</td>
<td>10</td>
<td>8</td>
<td>14</td>
<td>20</td>
</tr>
<tr>
<td>Akathisia events^</td>
<td>1</td>
<td>5</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Dyskinetic events^</td>
<td>4</td>
<td>0</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Residual events^</td>
<td>1</td>
<td>2</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Any extrapyramidal event</td>
<td>16</td>
<td>15</td>
<td>25</td>
<td>32</td>
</tr>
</tbody>
</table>

^ Patients with the following COSTART terms were counted in this category: dyskinesia, tardive dyskinesia.

Dystonia, Class Effect: Symptoms of dystonia, prolonged abnormal contractions of muscle groups, may occur in susceptible individuals during the first few days of treatment. Dystonic symptoms include: spasm of the neck muscles, sometimes progressing to tightness of the throat, swallowing difficulty, difficulty breathing, and/or protrusion of the tongue. While these symptoms can occur at low doses, the frequency and severity are greater with high potency and at higher doses of first generation antipsychotic drugs. In general, an elevated risk of acute dystonia may be observed in males and younger age groups receiving antipsychotics; however, events of dystonia have been reported infrequently (<1%) with olanzapine use.

6.3 Other Adverse Reactions

Local Injection Site Reactions

Eleven ZYPREXA RELPREVV-treated patients (3.6%) and 0 placebo-treated patients experienced treatment-emergent injection-related adverse reactions (injection site pain, buttlock pain, injection site mass, induration, injection site induration) in the placebo-controlled database. The most frequently occurring treatment-emergent adverse reaction was injection site pain (2.3% ZYPREXA RELPREVV-treated; 0% placebo-treated).

Other Adverse Reactions Observed During the Clinical Trial Evaluation of Olanzapine for Extended-Release Injectable Suspension

Injection site abscess has been reported in clinical trials with ZYPREXA RELPREVV therapy. Isolated cases required surgical intervention.

Commonly Observed Adverse Reactions During the Clinical Trial Evaluation of Olanzapine

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

ZYPREXA RELPREVV (olanzapine) for Extended Release Injectable Suspension

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Oral olanzapine administration was also associated with increases in serum prolactin [see Warnings and Precautions (5.17)], with an asymptomatic elevation of the eosinophil count in 0.3% of patients, and with an increase in CPK.

EEG Changes: Comparison of ZYPREXA RELPREVV and oral olanzapine, in a 24 week study, revealed no significant differences on EEG 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 EEG parameters, including QT, QTc, and PR intervals. Oral olanzapine use was associated with a mean increase in heart rate of 1 beats per minute with no change among placebo patients. The slight tendency to tachycardia may be related to olanzapine’s potential for inducing orthostatic changes [see Warnings and Precautions (5.11)].

6.4 Postmarketing Experience

Adverse reactions reported since market introduction that were temporally (but not necessarily causally) related to ZYPREXA therapy include the following: allergic reaction (e.g., cellulitis reaction, angioedema, pruritus or urticaria), cholestatic or mixed liver injury, diabolic coma, diabetic ketoacidosis, disorientation reaction (diphenhydramine, nsaids, or vomiting). Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), hepatitis, jaundice, neutropenia, pancreatitis, priapism, rash, restless legs syndrome, rhabdomyolysis, stuttering1, and venous thromboembolic events (including pulmonary embolism and deep venous thrombosis). Random cholesterol levels of ≥240 mg/dL and random triglyceride levels of ≥1000 mg/dL have been reported. Additionally, injection site abscesses has been reported in postmarketing reports with ZYPREXA RELPREVV therapy. Isolated cases required surgical intervention.

1 Stuttering was only studied in oral and long acting injection (LA) formulations.

7 DRUG INTERACTIONS

7.1 Potential for Other Drugs to Affect Olanzapine

Diazepam — The co-administration of diazepam with olanzapine potentiated the orthostatic hypotension observed with olanzapine [see Drug Interactions (7.2)].

Inhibitors of CYP1A2 — Fluvoxamine, a CYP1A2 inhibitor, decreases the clearance of olanzapine. This results in a mean increase in olanzapine Cmax following fluvoxamine of 54% in female nonsmokers and 77% in male smokers. The mean increase in olanzapine AUC is 52% and 108%, respectively. Lower doses of olanzapine should be considered in patients receiving concomitant treatment with fluvoxamine.

Inhibitors of CYP2D6 — Fluoxetine caused a small decrease in olanzapine clearance leading to a minimal change in olanzapine steady-state concentrations and, therefore dose adjustments are not routinely recommended but a 30% increase in the clearance of olanzapine may occur.

Warfarin — Warfarin (20 mg single dose) did not affect olanzapine pharmacokinetics [see Drug Interactions (7.2)].

7.2 Potential for Olanzapine to Affect Other Drugs

CNS Acting Drugs — Given the primary CNS effects of olanzapine, caution should be used when olanzapine is taken in combination with other centrally acting drugs and alcohol. Antihypertensive Agents — Olanzapine, because of its potential for inducing hypotension, may enhance the effects of certain antihypertensive agents.

Levodopa and Dopamine Agonists — Olanzapine may antagonize the effects of levodopa and dopamine agonists.

Lorazepam (LM) — Co-administration of lorazepam does not significantly affect the pharmacokinetics of olanzapine, unconjugated lorazepam, or total lorazepam. However, this co-administration of lorazepam with olanzapine potentiated the orthostatic hypotension observed with olanzapine [see Drug Interactions (7.2)].

Inducers of CYP1A2 or Gliclazide Transferase Enzymes — Omeprazole and rifampin may cause an increase in olanzapine clearance.

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Inducers of CYP1A2 or Gliclazide Transferase Enzymes — Omeprazole and rifampin may cause an increase in olanzapine clearance.

Lithium — Multiple doses of olanzapine (10 mg for 8 days) did not influence the kinetics of lithium. Therefore, concomitant olanzapine administration does not require dosage adjustment of lithium.

Valproate — Olanzapine (10 mg daily for 2 weeks) did not affect the steady-state plasma concentrations of valproate. Therefore, concomitant olanzapine administration does not require dosage adjustment of valproate.

Effect of Olanzapine on Drug Metabolizing Enzymes — In vitro studies utilizing human liver microsomes suggest that olanzapine has little potential to inhibit CYP1A2, CYP2C9, CYP2C19, CYP2D6, and CYP3A. Thus, olanzapine is unlikely to cause clinically important drug interactions mediated by these enzymes.

Imipramine — Single doses of olanzapine did not affect the pharmacokinetics of imipramine or its active metabolite desipramine.

Warfarin — Single doses of olanzapine did not affect the pharmacokinetics of warfarin [see Drug Interactions (7.1)].

Diazepam — Olanzapine did not influence the pharmacokinetics of diazepam or its active metabolite N-desmethyl-diazepam. However, diazepam co-administered with olanzapine increased the orthostatic hypotension observed with either drug given alone [see Drug Interactions (7.1)].

Alcohol — Multiple doses of olanzapine did not influence the kinetics of ethanol [see Drug Interactions (7.1)].

Biperiden — Multiple doses of olanzapine did not influence the kinetics of biperiden.

Theophylline — Multiple doses of olanzapine did not affect the pharmacokinetics of theophylline or its metabolites.

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8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic Effects, Pregnancy Category C — In oral reproduction studies in rats at doses up to 18 mg/kg/day and in rabbits at doses up to 30 mg/kg/day (9 and 30 times the maximum recommended human daily oral dose on a mg/m² basis, respectively) no evidence of teratogenicity was observed. In an oral rat teratology study, early resorptions and increased numbers of nonviable fetuses were observed at a dose of 18 mg/kg/day (9 times the maximum recommended human daily oral dose on a mg/m² basis). Gestation was prolonged at 10 mg/kg/day (5 times the maximum recommended human daily oral dose on a mg/m² basis). In an oral rabbit teratology study, fetal toxicity (manifested as increased resorptions and decreased fetal weight) occurred at a maternally toxic dose of 30 mg/kg/day (30 times the maximum recommended human daily oral dose on a mg/m² basis). No evidence of teratogenicity or embryo-fetal toxicity was observed in rats or rabbits with ZYPREXA RELPREVV. However, in a rabbit teratology study at 10 mg/kg/day (5 times the maximum recommended human dose of 300 mg every 2 weeks, respectively, on a mg/m² basis). Placental transfer of olanzapine occurred in rat pups.

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 resulting 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 benefit justifies the potential risk to the fetus.

Nonteratogenic Effects — Neonates exposed to antipsychotic drugs (including olanzapine), during the third trimester of pregnancy are at risk for extrapyramidal and/or withdrawal symptoms following delivery. There have been reports of agitation, hypertension, 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.

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 rats 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 1.9% 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 (5.7)).

Compared to patients from adult clinical trials, adolescents treated with oral ZYPREXA were likely to require higher weight-adjusted olanzapine doses than adults, 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, Dosage and Administration (2.1), and Warnings and Precautions (5.5)).

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 physical dependence or physical dependence in rats administered oral doses up to 15 times the maximum recommended human daily oral dose on a mg/m² basis.

Olanzapine has not 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 injections, and in approximately 2% of patients who received injections for up to 46 months. These reactions were reported with an unreported and possible potential of 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, aggressive behavior, delirium, possible neuroleptic malignant syndrome, respiratory depression/arrest, convulsion, hypertension, and hypotension. Eli Lilly and Company has reported cases of unexplained death in association with overdose of oral olanzapine alone. In one case of death, the amount of acutely ingested oral olanzapine was reported to be as low as 450 mg of oral 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-agonist activity, since beta stimulation may worsen hypotension in the setting of olanzapine-induced alpha blockade). Supportive therapy, including ventilation, may be required. Close medical supervision and monitoring should continue until the patient recovers.

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

11 DESCRIPTION

ZYPREXA RELPREVV is an atypical antipsychotic that belongs to the thienobenzodiazepine class. The chemical designation is 10H-thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-[[4-(4-methyl-1-piperazinyl)-4,4´-methylenebis[3-hydroxy-2-naphthalenecarboxylate]] (1:1), monohydrate. The formula is C₁₉H₁₄N₄O₇S•C₁₂H₂₄O₁₄•H₂O, which corresponds to a molecular weight of 716.8. The chemical structure is:

![Chemical Structure](image)

ZYPREXA RELPREVV is a long-acting form of olanzapine and is intended for deep intramuscular injection on a mg/m² basis.

ZYPREXA RELPREVV includes a vial of the drug product and a vial of the sterile diluent for ZYPREXA RELPREVV.

The drug product is olanzapine pamoate monohydrate, present as a yellow solid in a glass vial equivalent to 210, 300, or 405 mg olanzapine base per vial. The diluent for ZYPREXA RELPREVV is a clear, colorless to slightly yellow solution in a glass vial equivalent to 210, 300, or 405 mg olanzapine base per vial. The diluent contains benzyl alcohol and purified water.

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ZYPREXA RELPREVV (olanzapine)

For Extended Release Injectable Suspension

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Zyeprelx Relprev, ZYPR-0007-USPI-20180119_ZYPR-0001-MG-20161006
12.2 Pharmacodynamics
Olanzapine binds with high affinity to the following receptors: serotonin 5HT₂A/₂C, 5HT₆, (Kᵢ=4, 11, and 5 nM, respectively), dopamine D₁, D₂, D₃, D₄, and D₅ receptors (Kᵢ=7 nM), and adrenergic α₁, adrenergic α₂, and histamine H₁ receptors (Kᵢ=10 μM). Antagonism at receptors other than dopamine and 5HT may explain some of the other therapeutic and side effects of olanzapine. Olanzapine’s antagonism of muscarinic M₁, M₂, M₃, and M₅ receptors may provide a pharmacodynamic-like effect of conventional antipsychotics. Olanzapine’s antagonism of adrenergic receptors may explain the orthostatic hypotension observed with this drug. Olanzapine’s antagonism of adrenergic α₁ receptors may explain the orthostatic hypotension observed with this drug.

12.3 Pharmacokinetics
- The minimal pharmacokinetic properties of olanzapine are similar for a ZYPREXA RELPREVV and orally administered olanzapine. Refer to the section below describing the pharmacokinetics of orally administered olanzapine for details.

- Slow dissolution of ZYPREXA RELPREVV, a practically insoluble salt, after a deep intramuscular gluteal injection of a dose of ZYPREXA RELPREVV results in prolonged systemic olanzapine concentrations. Plasma concentrations that are sustained for periods of two weeks or more of injection every 2 or 4 weeks provides olanzapine plasma concentrations that are similar to those achieved by daily doses of oral olanzapine. The steady-state plasma concentrations for ZYPREXA RELPREVV for doses of 150 mg to 405 mg every 2 or 4 weeks are within the range of steady-state olanzapine plasma concentrations known to have been associated with oral doses of 5 mg to 20 mg olanzapine once daily. The change to a slow release, rate-controlled absorption process is the only fundamental pharmacokinetic difference between the administration of ZYPREXA RELPREVV and orally administered olanzapine. The effective half-life for olanzapine after intramuscular ZYPREXA RELPREVV administration is approximately 30 days as compared to the half-life after orally administered 30 hours. Olanzapine may persist for a period of months after a ZYPREXA RELPREVV injection. The long persistence of systemic concentrations of olanzapine may be an important consideration for the long-term clinical management of the patient. Typical systemic olanzapine plasma concentrations reach a plateau during the first 2 weeks of treatment and are at trough immediately prior to the next injection. The olanzapine plasma concentration fluctuation between the peak and trough is comparable to the peak and trough fluctuations associated with once daily oral dosing.

- Direct glucuronidation and cytochrome P450 (CYP) mediated oxidation are the major mechanisms of olanzapine metabolism. Approximately 25% of the dose is excreted unchanged, and 30% has been recovered in conjugated metabolites. Approximately 18% of the dose is excreted as direct glucuronidation, 9% as cytochrome P450 mediated oxidation, and 10% as conjugated metabolites. The major circulating metabolites were the 10-N-glucuronide, present at steady state at 44% of the dose administered, and 4´-N-desmethyl olanzapine, present at steady state at 31% of the concentration of olanzapine. Both metabolites lack pharmacological activity at the concentrations observed.

- Direct glucuronidation and cytochrome P450 (CYP) mediated oxidation are the major metabolic pathways for olanzapine. In vitro studies suggest that CYP 1A2 and 2D6, and the flavin-containing monoxygenase system are involved in olanzapine oxidation. CYP2D6 mediated oxidation appears to be a minor metabolic pathway in vivo, because the clearance of olanzapine is not reduced in patients who are deficient in this enzyme.

- Both olanzapine and its metabolites are available for intramuscular injection. One form (ZYPREXA RELPREVV) is described in this package insert. The other formulation (ZYPREXA IntraMuscular) is a solution of olanzapine. When ZYPREXA IntraMuscular is injected intramuscularly, olanzapine (as the free base) is rapidly absorbed and peak plasma concentrations occur within 15 to 45 minutes. With the exception of a higher maximal plasma concentration, the pharmacokinetics of ZYPREXA RELPREVV Exposure to ZYPREXA IntraMuscular are similar to those for orally administered olanzapine. Refer to the package insert for ZYPREXA IntraMuscular for additional information.

- Specific Populations — In general, the decision to use ZYPREXA RELPREVV in specific populations should be guided by age, concomitant disease, and concomitant medications. Patients who have never taken olanzapine, tolerability should be established with oral olanzapine 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 performed with caution in these patients [see Dosage and Administration (2.1)]. Precautions noted above for olanzapine apply to both forms of olanzapine.

- Renal Impairment — Because olanzapine is highly metabolized before excretion and only 7% of the drug is excreted unchanged, renal dysfunction alone is unlikely to have a major impact on the pharmacokinetics of olanzapine. The pharmacokinetic characteristics of orally administered olanzapine were similar in healthy volunteers and in subjects with normal renal function, indicating that dosage adjustment based upon the degree of renal impairment is not required. In addition, olanzapine is not removed by dialysis. The effect of renal impairment on olanzapine half-life has not been studied.

- Hepatic Impairment — Although the presence of hepatic impairment may be expected to reduce the clear rate of olanzapine, a study of liver function in subjects (n=6) with clinically significant (Childs Pugh Classification A and B) cirrhosis revealed little effect on the pharmacokinetics of orally administered olanzapine.

- Genetic — In a study involving 24 healthy subjects, the mean elimination half-life of olanzapine was about 1.5 times greater in smokers (21.1 ± 7.0 hours) 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 [see Dosage and Administration (2.1)].

- Gender — For both oral ZYPREXA and ZYPREXA RELPREVV higher average plasma concentrations of olanzapine were observed in women than in men. There were, however, no apparent differences between men and women in effectiveness or adverse effects. Dosage modifications based on gender should not be needed.

- Smoking Status — For both oral ZYPREXA and ZYPREXA RELPREVV, studies have demonstrated that the clearance of olanzapine is higher in smokers than in nonsmokers, although dosage modifications are not routinely recommended.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Carcinogenesis — Oral carcinogenicity studies were conducted in mice and rats. Olanzapine was administered to mice in two 78-week studies at doses of 3, 10, 30/20 mg/kg/day of ZYPREXA RELPREVV and orally administered olanzapine. The highest dose of ZYPREXA RELPREVV dose of 150 mg was lower than the maximum recommended human daily oral dose on a mg/m² basis; 0.25, 2, 8 mg/kg/day (equivalent to 0.8-2.6 times the maximum recommended human daily oral dose on a mg/m² basis). Rats were dosed for 2 years at doses of 0.25, 1.25, 4 mg/kg/day (males) and 0.25, 1, 4, 8 mg/kg/day (females) (equivalent to 0.1-3.2 and 0.13-4 times the maximum recommended human daily oral dose on a mg/m² basis, respectively). The incidence of liver hemangiosarcomas and hemangioendotheliomas was significantly increased in male mice at doses of 8 mg/kg/day and in female rats at doses of 4 mg/kg/day, respectively. The incidence of liver hemangiosarcoma and hemangioendotheliomas was significantly increased in 1 mouse study in female mice dosed at 8 mg/kg/day (2 times the maximum recommended human daily oral dose on a mg/m² basis). These tumors were not increased in another mouse study in females dosed at 10 or 30/20 mg/kg/day (2.5 times the maximum recommended human daily oral dose on a mg/m² basis); in this study, there was a high incidence of early mortality in males of the 30/20 mg/kg/day group. The incidence of mammary gland adenomas and adenocarcinomas was significantly increased in female mice dosed at ≥2 mg/kg/day and 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). Rats were also treated with ZYPREXA RELPREVV once a month for 2 years at doses of 5, 10, 20 mg/kg (males) and 10, 25, 50 mg/kg (females) (equivalent to 0.08-0.8 times the maximum recommended human dose of 300 mg every 2 weeks on a mg/kg basis; dosing was limited due to local reactions at the IM injection site). The incidence of tumors in this study was not altered when compared to ZYPREXA RELPREVV dosed for 1 month with a peak body weight of 22.4 mg/kg/day. The incidence of tumors was not altered when compared to ZYPREXA RELPREVV dosed for 1 month with a peak body weight of 22.4 mg/kg/day. The incidence of tumors was not altered when compared to ZYPREXA RELPREVV dosed for 1 month with a peak body weight of 22.4 mg/kg/day. The incidence of tumors was not altered when compared to ZYPREXA RELPREVV dosed for 1 month with a peak body weight of 22.4 mg/kg/day.
10 mg/kg developed reversible neutropenia and/or reversible hemolytic 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) 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 bone marrow changes were found in any of the species examined. Bone marrow was normocellular or hypercellular, 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 patients (n=404) who were experiencing psychotic symptoms, consistent 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 bone marrow changes were found in any of the species examined. Bone marrow was normocellular or hypercellular, indicating that the reductions in circulating blood cells were probably due to peripheral (non-marrow) factors.

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

Patients and caregivers should be advised that elderly patients with dementia-related psychosis should be closely monitored following injection with ZYPREXA RELPREVV. Due to the risk of CVAEs and associated mortality, ZYPREXA RELPREVV should not be administered to patients with dementia-related psychosis treated with ZYPREXA RELPREVV if there is a significant increase in the risk of CVAEs or if the patient is at risk for CVAEs. Patients and caregivers should be advised that elderly patients with dementia-related psychosis treated with ZYPREXA RELPREVV had a significantly higher incidence of cerebrovascular adverse events (e.g., stroke, transient ischemic attack) compared with placebo.

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 dysrhythmia) [see Warnings and Precautions (5.5)].

17.5 Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)

Patients should be advised to report to their health care provider at the earliest onset of any signs or symptoms that may be associated with Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) [see Warnings and Precautions (5.6)].

17.6 Hyperglycemia and Diabetes Mellitus

Patients should be advised of the potential risk of hyperglycemia-related adverse reactions related to ZYPREXA RELPREVV. 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 RELPREVV [see Warnings and Precautions (5.7)].

17.7 Dyslipidemia

Patients should be counseled that dyslipidemia has occurred during treatment with ZYPREXA RELPREVV. Patients should have their lipid profile monitored regularly [see Warnings and Precautions (5.7)].

17.8 Weight Gain

Patients should be counseled that weight gain has occurred during treatment with ZYPREXA RELPREVV. Patients should have their weight monitored regularly [see Warnings and Precautions (5.7)].

17.9 Orthostatic Hypotension

Patients should be advised of the risk of orthostatic hypotension, and in association with the use of other drugs that may potentiate the orthostatic effect of ZYPREXA RELPREVV, e.g., diazepam 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, fast or slow heartbeat, or fainting.

17.10 Potential for Cognitive and Motor Impairment

Because ZYPREXA RELPREVV 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 RELPREVV 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 after each injection [see Dosage and Administration (2.1) and Warnings and Precautions (5.1, 5.14)].

17.11 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)].

17.12 Concomitant Medication

Patients should be advised to inform their physicians if they are taking, or plan to take,.ZYPREXA RELPREVV (olanzapine) (olanzapine monohydrate) or Symbyax® (olanzapine/fluoxetine 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)].

17.13 Alcohol

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

17.14 Use in Specific Populations

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

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

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

Literature revised January 19, 2018

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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.

Call your doctor if you have any of these symptoms of high blood sugar (hyperglycemia) while taking ZYPREXA RELPREVV:
   - feel very thirsty
   - need to urinate more than usual
   - feel very hungry
   - feel weak or tired
   - feel sick to your stomach
   - feel confused or your breath smells fruity

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)
For Extended Release Injectable Suspension ZYPR-0001-MG-20161006
ZYPREXA RELPREVV (olanzapine)

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

• are pregnant or plan to become pregnant. It is not known if ZYPREXA RELPREVV will harm your unborn baby.
• are breast-feeding or plan to breast-feed. ZYPREXA RELPREVV can pass into your breast milk and may harm your baby. You should not breast-feed while taking ZYPREXA RELPREVV. Talk to your doctor about the best way to feed your baby if you take ZYPREXA RELPREVV.

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 RELPREVV 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 RELPREVV with your other medicines. Do not start or stop any medicine while taking ZYPREXA RELPREVV without talking to your doctor first.

**How should I receive ZYPREXA RELPREVV?**

• ZYPREXA RELPREVV will be injected into the muscle in your buttck (gluteus) by your doctor or nurse at the clinic.
• After receiving ZYPREXA RELPREVV, 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 RELPREVV.

**What should I avoid while receiving ZYPREXA RELPREVV?**

• ZYPREXA RELPREVV 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 RELPREVV 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 RELPREVV. Drinking alcohol while you take ZYPREXA RELPREVV may make you sleepier than if you take ZYPREXA RELPREVV alone.

**What are the possible side effects of ZYPREXA RELPREVV?**

**Serious side effects may happen when you take ZYPREXA RELPREVV, including:**

• See “What is the most important information I should know about ZYPREXA RELPREVV?”, 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 RELPREVV 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 RELPREVV. 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
• Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS): DRESS can occur with ZYPREXA RELPREVV. Features of DRESS may include rash, fever, swollen glands and other internal organ involvement such as liver, kidney, lung and heart. DRESS is sometimes fatal; therefore, tell your doctor immediately if you experience any of these signs.
• 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 RELPREVV. It may also start after you stop taking ZYPREXA RELPREVV. 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.
• Seizures: Tell your doctor if you have a seizure during treatment with ZYPREXA RELPREVV.
• 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 RELPREVV 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 RELPREVV. 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 RELPREVV

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide.

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

What are the ingredients in ZYPREXA RELPREVV?

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.