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
Order is forwarded to Lilly/Specialty Distributor
Lilly/Specialty Distributor verifies Pharmacy Service Provider eligibility via the on-line system
Pharmacy Service Provider receives ZYPREXA RELPREVV
If eligibility is confirmed, Lilly/Specialty Distributor ships # units ordered of ZYPREXA RELPREVV

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

Key
- Prescriber Activities
- Healthcare Facility Activities
- Pharmacy Service Provider Activities

a 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
For questions regarding the Patient Care Program or to enroll, please contact the Patient Care Program Coordinating Center:

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

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

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

**Via Internet:** www.zyprexarelprevvprogram.com
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.

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

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.
Prescriber Information

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

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

Three Steps to Patient Enrollment:

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

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

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

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

Patient Care Program Data Entry

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

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

Via Telephone: 1-877-772-9390
Via Fax: 1-877-772-9391
Via Internet: www.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 prescriber will see only their associated patients and the option to enroll new patients.
3. Select:
   • The appropriate patient for whom he/she is entering data.
   • Or the option to enroll a new patient.
4. The system will prompt the prescriber to enter enrollment data for a new patient, or PDSS data for an already enrolled patient.

After enrollment is complete, a unique Patient Identification Number (PIN) and a healthcare facility unique identifier will be provided to the prescriber via a patient authorization notification fax or email. The prescriber should provide the patient’s PIN and healthcare facility unique identifier with the first prescription to assist the pharmacy service provider in completing its ZYPREXA RELPREVV Patient Care Program responsibilities.
Healthcare Facility Information

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

Authorized Healthcare Facility Representative

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

Patient Care Program Data Entry

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

Three Steps to Healthcare Facility Enrollment:

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

**Pharmacy Service Provider Information**

**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**

- 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)

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/re fill 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 convenience kit leaving the pharmacy.
• I understand that the ZYPREXA RELPREVV Patient Care Program Coordinating Center may contact the pharmacy to clarify information provided or to obtain information about the patient.
• I will comply with audits by the manufacturer or a third party acting on behalf of the manufacturer to ensure all processes and procedures are in place and being followed.
• I will maintain records of all processes and procedures including compliance with those processes and procedures.

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.

Date: ___________  ___________  ___________  ___________

Administrator Signature

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

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

**HEALTHCARE FACILITY INFORMATION**

- [ ] Enrollment
- [ ] Reenrollment

Healthcare Facility Name: _____________________________________________________________

Please specify location of Healthcare Facilities:  
- [ ] Prescriber Office  
- [ ] Clinic/Outpatient Facility  
- [ ] Hospital  
- [ ] Other

Address: ___________________________________________________________________________

City: ___________________________________________  
State: ________  
Zip: ____________________________________________

Phone: ___________________________  
Fax: _________________________________

**AUTHORIZED HEALTHCARE FACILITY REPRESENTATIVE INFORMATION**

First Name: ___________________________________________  
MI: _______  
Last Name: __________________________________________

Position/Title: ____________________________________________________________________

Phone: ___________________________  
Fax: _________________________________

Email: ___________________________________________________________________________

Preferred Method of Communication:  
- [ ] Email  
- [ ] Fax

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

Delegate First Name: _____________________________  
MI: _______  
Last Name: _______________________________________

Facility Name: ______________________________________________________________________

Phone: ___________________________  
Fax: _________________________________

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

Email: ___________________________________________________________________________

Delegate First Name: _____________________________  
MI: _______  
Last Name: _______________________________________

Facility Name: ______________________________________________________________________

Phone: ___________________________  
Fax: _________________________________

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

Email: ___________________________________________________________________________

Delegate First Name: _____________________________  
MI: _______  
Last Name: _______________________________________

Facility Name: ______________________________________________________________________

Phone: ___________________________  
Fax: _________________________________

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

Email: ___________________________________________________________________________

Delegate First Name: _____________________________  
MI: _______  
Last Name: _______________________________________

Facility Name: ______________________________________________________________________

Phone: ___________________________  
Fax: _________________________________

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

Email: ___________________________________________________________________________

Delegate First Name: _____________________________  
MI: _______  
Last Name: _______________________________________

Facility Name: ______________________________________________________________________

Phone: ___________________________  
Fax: _________________________________

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

Email: ___________________________________________________________________________

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

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

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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 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 ensure the healthcare 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 healthcare setting to clarify information provided or to obtain information about the patient.

- I will comply with audits by the manufacturer or a third party acting on behalf of the manufacturer to ensure all processes and procedures are in place and being followed.

- I will maintain records of all processes and procedures including compliance with those processes and procedures.

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

Date: ________________

month   day   year

Authorized Healthcare Facility Representative Name (print) _______________________________ Title ______________________________

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

**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:**

**Date of Injection**

<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient No.:</strong> (PIN)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Patient Name:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>First Name</strong></td>
<td><strong>Mi</strong></td>
<td><strong>Last Name</strong></td>
</tr>
<tr>
<td><strong>Date of Birth:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>month</strong></td>
<td><strong>day</strong></td>
<td><strong>year</strong></td>
</tr>
<tr>
<td><strong>PDSS since last visit?</strong> (check one)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>If Yes, has the prescriber been notified of the PDSS event?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Time of Injection</strong> (24-hour clock)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dose of Injection</strong> (check one)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>150 mg</td>
<td>210 mg</td>
<td>300 mg</td>
</tr>
<tr>
<td><strong>Observed at least 3 hours post-injection?</strong> (check one)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>PDSS during onsite observation?</strong> (check one)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>If Yes, has the prescriber been notified of the PDSS event?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>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?</strong> (check one)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Following the injection, was the patient accompanied from the facility?</strong> (check one)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Signature</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Healthcare Facility Staff Member Signature</td>
<td>Healthcare Facility Staff Member Signature</td>
<td>Healthcare Facility Staff Member Signature</td>
</tr>
<tr>
<td><strong>Was the patient or legal guardian given a Medication Guide prior to this injection?</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

---

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

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

www.zyprexarelprevvprogram.com

Version 2.0 03Aug2012

CONFIDENTIAL

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Patient Registration Form Copy

Provide this copy of the ZYPREXA RELPREVV Patient Care Program Patient Registration Form to the patient or guardian upon enrollment.

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 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.
PATIENT REGISTRATION 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: ___________________
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.

________________________________________________________
Signature

________________________________________________________
Printed Name of Patient

________________________________________________________
Printed Name of Legal Guardian (if applicable)

☐ Check the box if the patient has not signed due to enrollment decision being made by prescriber who is authorized via a court order.
  Date of Court Order Expiration (MMDDYYYY) ______________________________

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

________________________________________________________
Signature of Prescriber

________________________________________________________
Printed Name of Prescriber

PHONE 1-877-772-9390    FAX 1-877-772-9391    www.zyprexarelprevvprogram.com
Does the patient have a diagnosis of schizophrenia?  
☐ Yes  ☐ No

**PATIENT/INJECTION INFORMATION**

Date of Injection:  

Day  

Month  

Year

Time of ZYPREXA RELPREVV Injection:  

:  

24-hour clock

Convenience Kit Package

Lot #  


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

☐ 1 - 15 minutes  ☐ 46 - 60 minutes  ☐ 121 - 150 minutes (2 ½ hours)

☐ 16 - 30 minutes  ☐ 61 - 90 minutes (1 ½ hours)  ☐ 151 - 180 minutes (3 hours)

☐ 31 - 45 minutes  ☐ 91 - 120 minutes (2 hours)  ☐ If greater than 3 hours please specify:

☐ 12 - 30 minutes  ☐ 61 - 90 minutes (1 ½ hours)

☐ Other dose _____ mg

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  ☐ Coma  ☐ Hypertension  ☐ Tachycardia

☐ Agitation  ☐ Confusion  ☐ Hypotension  ☐ Various extrapyramidal symptoms

☐ Anxiety  ☐ Convulsion/Seizure  ☐ Other cognitive impairment  ☐ Weakness

☐ Aspiration  ☐ Delirium  ☐ Possible neuroleptic malignant syndrome  ☐ Other _____

☐ Ataxia  ☐ Disorientation  ☐ Reduced level of consciousness  ☐ Other _____

☐ Cardiac arrhythmias  ☐ Dizziness  ☐ Respiratory depression  ☐ Other _____

☐ Cardiopulmonary arrest  ☐ Dysarthria  ☐ Sedation  ☐ Other _____

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FAX 1-877-772-9391  

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Patient No.: [ ] [ ] [ ] [ ] [ ] (PIN)

Patient Name: ____________________________

First Name ____________________________ MI ____________________________ Last Name ____________________________

PDSS start date: [ ] [ ] [ ] – [ ] [ ] [ ] – [ ] [ ] [ ]

month day year

PDSS resolution date: [ ] [ ] [ ] – [ ] [ ] [ ] – [ ] [ ] [ ] 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>
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<td></td>
</tr>
</tbody>
</table>

Phone 1-877-772-9390

FAX 1-877-772-9391

www.zyprexarelprevvprogram.com
Patient No.:  
(PIN)  

Patient Name: _________________________________________      _________  
                                                                 ___________________________________________  

First Name                                                                            MI                      Last Name  

POST-INJECTION DELIRIUM/SEDATION SYNDROME (PDSS) FORM  

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

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

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

HISTORY PRIOR TO PDSS EVENT  

Does the patient have any relevant comorbidities?  
☐ Yes - Please specify:  
__________________________________________________________________________________________________  
☐ No  

PRIOR MEDICATIONS  

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

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

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

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

Event reported by:  
First  MI  Last  
__________________________________________________________________________  

Title/Occupation:  
__________________________________________________________________________  

If agent of the Prescriber, name of Prescriber:  
__________________________________________________________________________
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.

<table>
<thead>
<tr>
<th>PHARMACY INFORMATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Enrollment ☐ Reenrollment</td>
</tr>
<tr>
<td>Pharmacy/Hospital Name: ____________________________________________________________</td>
</tr>
<tr>
<td>Pharmacy DEA Number: ________________________________________________________________</td>
</tr>
<tr>
<td>Please specify description of Pharmacy: ☐ Community/Retail ☐ Specialty Pharmacy ☐ Hospital or Institution ☐ Other</td>
</tr>
<tr>
<td>Address Line 1: ________________________________________________________________</td>
</tr>
<tr>
<td>Address Line 2: ________________________________________________________________</td>
</tr>
<tr>
<td>City: ____________________ State: __________ Zip: ________________</td>
</tr>
<tr>
<td>Primary Phone: ____________________ Secondary Phone: ____________________</td>
</tr>
<tr>
<td>Fax: ____________________</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SHIP TO INFORMATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ship To Address (if the same as above, check here) ☐</td>
</tr>
<tr>
<td>Ship To Contact Name: ____________________________________________________________</td>
</tr>
<tr>
<td>Address Line 1: ________________________________________________________________</td>
</tr>
<tr>
<td>Address Line 2: ________________________________________________________________</td>
</tr>
<tr>
<td>City: ____________________ State: __________ Zip: ________________</td>
</tr>
<tr>
<td>Primary Phone: ____________________ Secondary Phone: ____________________</td>
</tr>
<tr>
<td>Fax: ____________________</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PHARMACIST-IN-CHARGE INFORMATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Name: ____________________ MI: _____ Last Name: ____________________</td>
</tr>
<tr>
<td>Email: ____________________</td>
</tr>
<tr>
<td>Phone: ____________________ (if different from above) Fax: ____________________ (if different from above)</td>
</tr>
</tbody>
</table>

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 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/ill 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 convenience kit leaving the pharmacy.
- I understand that the ZYPREXA RELPREVV Patient Care Program Coordinating Center may contact the pharmacy to clarify information provided or obtain information about the patient.
- I will comply with audits by the manufacturer or a third party acting on behalf of the manufacturer to ensure all processes and procedures are in place and being followed.
- I will maintain records of all processes and procedures including compliance with those processes and procedures.

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: [ ] [ ] [ ]

PHONE 1-877-772-9390 FAX 1-877-772-3939 www.zyprexarelprevvprogram.com

Version 5.0 20Aug2021

CONFIDENTIAL
PRESERVER 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

PRESERVER 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

Date:  ____________  ____________  ____________

month  day  year
INJECTION

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.

Patient No.:

Patient Name: _________________________________________

First                                                                                      MI                      Last

Date of Birth: month ~ day ~ year

PDSS since the last visit? (After the patient left the office, following his/her previous injection, did the patient experience post-injection delirium/sedation syndrome?)

☐ No    ☐ Yes

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

☐ Yes    ☐ No

ZYPREXA RELPREVV TREATMENT

Date of Injection: month ~ day ~ year

Time of ZYPREXA RELPREVV injection: 24-hour clock

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

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

Did the patient experience post-injection delirium/sedation syndrome during the onsite post-injection observational period?

☐ No    ☐ Yes

If Yes, has the prescriber been notified of the PDSS event? ☐ Yes    ☐ No

Following the injection, was the patient alert, oriented, and absent of any signs and symptoms of PDSS prior to being released from the healthcare facility?

☐ Yes    ☐ No

Following the injection, was the patient accompanied from the facility?

☐ Yes    ☐ No    ☐ Not applicable, patient did not leave facility (in-patient)

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

Healthcare Facility Staff Member Signature

Healthcare Facility Staff Member Name (print): __________________________

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

Version 2.0 03Aug2012 CONFIDENTIAL
Patients are at risk for severe sedation (including coma) and/or delirium after each injection and must

Hyperglycemia and Diabetes Mellitus:

Diazepam:

Establish tolerability with oral olanzapine prior to initiating trea

Alcohol:

Weight Gain:

Tardive Dyskinesia:

Carbamazepine:

• Efficacy was established in two clinical trials in patients with schizophrenia: one 8-week trial in adults and one

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ZYPREXA RELPREVV (olanzapine)

For Extended Release Injectable Suspension

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Revised: 2/2021

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

See all 15 pages to view full prescribing information.
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, including sedation (ranging from mild in severity to 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), Overdosage (10.1), and Patient Counseling Information (17)].

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) in patients with dementia related psychosis largely in patients taking antipsychotic drugs, 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 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 [see Warnings and Precautions (5.3), Use in Specific Populations (8.5) and Patient Counseling Information (17)].

1 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.

1.1 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 gluteal 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 package insert for ZYPREXA IntraMuscular for more information about this 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 gluteal 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

<table>
<thead>
<tr>
<th>Target Oral ZYPREXA Dose</th>
<th>Dosing of ZYPREXA RELPREVV During the First 8 Weeks</th>
<th>Maintenance Dose After 8 Weeks of 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 Based Warning, Warnings and Precautions (5.1), and

Overdosage (10.1)]. Patients should be informed of this risk and how to recognize related symptoms [see Patient Counseling Information (17)]. ZYPREXA RELPREVV must be administered in a registered healthcare facility 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 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, aggression, dizziness, weakness, hypertension, and convulsion. 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 Overdosage (10)].

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 wk 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 (5.1), Drug Interactions (7), and Clinical Pharmacology (12.3)].

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

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 gluteal 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:

• Single-dose 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>1.6 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 needlstick injury. Loosen the powder by lightly tapping the vial. Open the prepackaged Hypodermic Needle-Pro syringe and needle with needle protection device.

ZYPREXA RELPREVV (olanzapine) For Extended Release Injectable Suspension ZYP-0012-USPI-20210222 ZYP-0012-USPI-20210222

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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.

Shake the vial vigorously until the suspension appears smooth and is consistent in color and texture. The suspended product will be yellow and opaque (see Figure 3).

Figure 3: 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 at room temperature for up to 24 hours in the 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>

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 the 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-dose 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 in a pharmaceutically acceptable excipient (not for single-dose injection) to yield a solution with a pH of 3.5. 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 delirium or 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, delirium, 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)].

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)]. 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 1-877-777-9390.

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 cardiorespiratory 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, Use in Specific Populations (8.5), and Patient Counseling Information (17)]. In placebo-controlled oral olanzapine clinical trials of elderly patients with dementia-related psychosis, the incidence of death in olanzapine-treated patients was significantly greater than placebo-treated patients (3.5% vs 1.5%, respectively).

Cerebrovascular Adverse Events (CVEs), Including Stroke

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...
Olanzapine-treated subjects 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=596). 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</th>
<th>Up to 12 weeks exposure</th>
<th>At least 48 weeks exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Glucose</td>
<td></td>
<td></td>
<td>N</td>
<td>Patients</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>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo</td>
<td>293</td>
<td>3.4%</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>14.7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo</td>
<td>96</td>
<td>11.5%</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 9–12 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 RELPREVV have not been established for at least 18 years.

In an analysis of 3 placebo-controlled 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 Olanzapine Monotherapy Studies

<table>
<thead>
<tr>
<th>Laboratory Analyte</th>
<th>Category Change (at least once) from Baseline</th>
<th>Treatment</th>
<th>Up to 12 weeks exposure</th>
<th>At least 48 weeks exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Glucose</td>
<td></td>
<td></td>
<td>N</td>
<td>Patients</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>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo</td>
<td>53</td>
<td>1.9%</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>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo</td>
<td>13</td>
<td>0.0%</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)).

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, 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 from normal or borderline to low, was greater in long-term studies (at least 48 weeks) as compared with short-term studies. Table 4 shows categorical changes in fasting lipids values.
In phase 1 of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE), over a median exposure of 9.2 months, the mean increase in total cholesterol was 4.9 mg/dL. Phase 1 of CATIE, the mean increase in total cholesterol was 4.9 mg/dL. Dose group differences with respect to increases in fasting triglycerides have been 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. In long-term studies, at least 24 weeks, adolescents had increases from baseline in mean fasting total cholesterol, LDL cholesterol, and triglycerides of 4.5 mg/dL. Table 5 shows categorical changes in fasting lipids values in adolescents.

Table 4: Changes in Fasting Lipids Values from Adolescent 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 Triglycerides</td>
<td>Increase by ≥50 mg/dL</td>
<td>Olanzapine</td>
<td>457</td>
<td>10.7%</td>
<td>424</td>
<td>45.9%</td>
</tr>
<tr>
<td></td>
<td>Normal to High (&lt;170 mg/dL to ≥200 mg/dL)</td>
<td>Olanzapine</td>
<td>361</td>
<td>5.0%</td>
<td>351</td>
<td>42.3%</td>
</tr>
<tr>
<td></td>
<td>Borderline to High (≥150 mg/dL to &lt;200 mg/dL)</td>
<td>Olanzapine</td>
<td>93</td>
<td>8.3%</td>
<td>71</td>
<td>24.4%</td>
</tr>
<tr>
<td></td>
<td>Normal to High (&lt;170 mg/dL to ≥200 mg/dL)</td>
<td>Placebo</td>
<td>361</td>
<td>5.0%</td>
<td>351</td>
<td>42.3%</td>
</tr>
<tr>
<td></td>
<td>Borderline to High (≥150 mg/dL to &lt;200 mg/dL)</td>
<td>Placebo</td>
<td>93</td>
<td>8.3%</td>
<td>71</td>
<td>24.4%</td>
</tr>
<tr>
<td>Fasting LDL Cholesterol</td>
<td>Increase by ≥30 mg/dL</td>
<td>Olanzapine</td>
<td>361</td>
<td>14.3%</td>
<td>351</td>
<td>28.7%</td>
</tr>
<tr>
<td></td>
<td>Normal to High (&lt;100 mg/dL to ≥130 mg/dL)</td>
<td>Olanzapine</td>
<td>85</td>
<td>4.2%</td>
<td>84</td>
<td>10.4%</td>
</tr>
<tr>
<td></td>
<td>Borderline to High (≥100 mg/dL to &lt;160 mg/dL)</td>
<td>Olanzapine</td>
<td>361</td>
<td>14.3%</td>
<td>351</td>
<td>28.7%</td>
</tr>
<tr>
<td></td>
<td>Normal to High (&lt;100 mg/dL to ≥130 mg/dL)</td>
<td>Placebo</td>
<td>85</td>
<td>4.2%</td>
<td>84</td>
<td>10.4%</td>
</tr>
<tr>
<td></td>
<td>Borderline to High (≥100 mg/dL to &lt;160 mg/dL)</td>
<td>Placebo</td>
<td>361</td>
<td>14.3%</td>
<td>351</td>
<td>28.7%</td>
</tr>
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</table>

Table 5: Changes in Fasting Lipids Values from Adolescent Olanzapine Monotherapy Studies (Cont.)

<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 Triglycerides</td>
<td>Increase by ≥50 mg/dL</td>
<td>Olanzapine</td>
<td>457</td>
<td>10.7%</td>
<td>424</td>
<td>45.9%</td>
</tr>
<tr>
<td></td>
<td>Normal to High (&lt;170 mg/dL to ≥200 mg/dL)</td>
<td>Olanzapine</td>
<td>361</td>
<td>5.0%</td>
<td>351</td>
<td>42.3%</td>
</tr>
<tr>
<td></td>
<td>Borderline to High (≥150 mg/dL to &lt;200 mg/dL)</td>
<td>Olanzapine</td>
<td>93</td>
<td>8.3%</td>
<td>71</td>
<td>24.4%</td>
</tr>
<tr>
<td></td>
<td>Normal to High (&lt;170 mg/dL to ≥200 mg/dL)</td>
<td>Placebo</td>
<td>361</td>
<td>5.0%</td>
<td>351</td>
<td>42.3%</td>
</tr>
<tr>
<td></td>
<td>Borderline to High (≥150 mg/dL to &lt;200 mg/dL)</td>
<td>Placebo</td>
<td>93</td>
<td>8.3%</td>
<td>71</td>
<td>24.4%</td>
</tr>
</tbody>
</table>

Table 6: Weight Gain with Olanzapine Use in Adults

<table>
<thead>
<tr>
<th>Arm N Patients</th>
<th>N Patients</th>
<th>N Patients</th>
<th>N Patients</th>
<th>N Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 Weeks (N=7465) (%)</td>
<td>6 Months (N=4162) (%)</td>
<td>12 Months (N=1345) (%)</td>
<td>24 Months (N=474) (%)</td>
<td>36 Months (N=147) (%)</td>
</tr>
<tr>
<td>6 Weeks (N=7465) (%)</td>
<td>6 Months (N=4162) (%)</td>
<td>12 Months (N=1345) (%)</td>
<td>24 Months (N=474) (%)</td>
<td>36 Months (N=147) (%)</td>
</tr>
<tr>
<td>6 Weeks (N=7465) (%)</td>
<td>6 Months (N=4162) (%)</td>
<td>12 Months (N=1345) (%)</td>
<td>24 Months (N=474) (%)</td>
<td>36 Months (N=147) (%)</td>
</tr>
<tr>
<td>6 Weeks (N=7465) (%)</td>
<td>6 Months (N=4162) (%)</td>
<td>12 Months (N=1345) (%)</td>
<td>24 Months (N=474) (%)</td>
<td>36 Months (N=147) (%)</td>
</tr>
<tr>
<td>6 Weeks (N=7465) (%)</td>
<td>6 Months (N=4162) (%)</td>
<td>12 Months (N=1345) (%)</td>
<td>24 Months (N=474) (%)</td>
<td>36 Months (N=147) (%)</td>
</tr>
<tr>
<td>6 Weeks (N=7465) (%)</td>
<td>6 Months (N=4162) (%)</td>
<td>12 Months (N=1345) (%)</td>
<td>24 Months (N=474) (%)</td>
<td>36 Months (N=147) (%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Amount Gained (kg)</th>
<th>6 Weeks (N=7465) (%)</th>
<th>6 Months (N=4162) (%)</th>
<th>12 Months (N=1345) (%)</th>
<th>24 Months (N=474) (%)</th>
<th>36 Months (N=147) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤5</td>
<td>26.2</td>
<td>24.3</td>
<td>20.8</td>
<td>23.2</td>
<td>17.0</td>
</tr>
<tr>
<td>&gt;5 to ≤10</td>
<td>17.6</td>
<td>24.9</td>
<td>24.7</td>
<td>24.1</td>
<td>18.4</td>
</tr>
<tr>
<td>&gt;10 to ≤15</td>
<td>11.8</td>
<td>14.9</td>
<td>11.4</td>
<td>17.0</td>
<td>14.7</td>
</tr>
<tr>
<td>&gt;15 to ≤20</td>
<td>8.6</td>
<td>8.3</td>
<td>9.3</td>
<td>11.6</td>
<td>7.9</td>
</tr>
<tr>
<td>&gt;20 to ≤25</td>
<td>5.1</td>
<td>3.3</td>
<td>5.1</td>
<td>4.1</td>
<td>1.1</td>
</tr>
<tr>
<td>&gt;25 to ≤30</td>
<td>2.3</td>
<td>2.3</td>
<td>2.3</td>
<td>2.3</td>
<td>2.3</td>
</tr>
<tr>
<td>&gt;30 (&gt;66)</td>
<td>0.8</td>
<td>1.2</td>
<td>1.2</td>
<td>1.2</td>
<td>1.2</td>
</tr>
</tbody>
</table>

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 RELPREV, mean baseline-to-endpoint increase in weight (150 mg/2 weeks, n=140: 0.67 kg; 405 mg/4 weeks, n=315: 0.89 kg; 300 mg/2 weeks, n=140: 1.70 kg) was observed with significant differences between the lowest and highest dose groups (150 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. ZYPREXA RELPREV have not been established in patients under the age of 18 years.
Table 7: Weight Gain with Oral Olanzapine Use in Adolescents

<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>&lt;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>24.8</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 8: Weight Gain with Olanzapine Use in Adolescents

<table>
<thead>
<tr>
<th>Mean change in body weight from baseline (median exposure = 3 weeks)</th>
<th>Olanzapine-treated patients</th>
<th>Placebo-treated patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of patients who gained at least 7% of baseline body weight</td>
<td>46.0% (median exposure to 7% = 4 weeks)</td>
<td>9.8% (median exposure to 7% = 8 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>
<td>2.7% (median exposure to 15% = 8 weeks)</td>
</tr>
</tbody>
</table>

5.8 Tardive Dyskinesia

A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of antipsychotic treatment, which patients are likely to develop the syndrome. Whether antipsychotic drug products differ in their potential to cause tardive dyskinesia is unknown.

The risk of developing tardive dyskinesia and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses or may even arise after discontinuation of treatment.

Tardive dyskinesia may remit, partially or completely, if antipsychotic treatment is withdrawn. However, treatment, itself, may not suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying process. The effect that suppressive suppression has upon the long-term course of the syndrome is unknown.

5.9 Orthostatic Hypotension

Olanzapine may induce orthostatic hypotension associated with dizziness, tachycardia, bradycardia and, in some patients, syncope, probably reflecting its α-adrenergic antagonistic properties [see Patient Counseling Information (17)]. Syncope-related adverse reactions were reported in 0.1% of patients treated with ZYPREXA RELPREV in clinical studies.

5.10 Falls

ZYPREXA RELPREV 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.
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% [48/2400] of females), sexual function-related events2 (2% [155/8136] of females and males), and breast-related events3 (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 events3 (2% [3/168] of females, 2% [7/288] of males) [see Use in Specific Populations (8.4)].

1 Based on a search of the following terms: amenorrhea, hypomenorrhea, menstruation delayed, and oligomenorrhea.
2 Based on a search of the following terms: anorgasms, 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 RELPREV, statistically significant differences among dose groups were observed for prolactin levels, with a mean baseline-to-endpoint increase observed in the highest dose group (300 mg/2 weeks, n=115: 3.57 ng/mL) relative to mean decreases in the lower dose groups (150 mg/2 weeks, n=109: -5.61 ng/mL; 405 mg/4 weeks, n=259: -2.76 ng/mL). In a single 6-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, 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 20 mg/day and 20 vs 40 mg/day.

5.18 Laboratory Tests

Fasting glucose blood 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 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect or predict the rates observed in practice.

The information below for ZYPREXA RELPREV is derived primarily from a clinical trial database consisting of 2058 patients with approximately 1948 patient years of exposure to ZYPREXA RELPREV. 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 below. Adverse reactions were assessed by the collection of adverse reactions, vital signs, weights, laboratory analytes, ECGs, and the results of physical and ophthalmologic examinations. In the tables and tabulations that follow for ZYPREXA RELPREV, the MedDRA terminology has been used to classify reported 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 profile of ZYPREXA RELPREV.

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 healthcare provider 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 RELPREV (4%; 13/306 patients) and placebo (5%; 5/98 patients) 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 greater in at least one of the ZYPREXA RELPREV treatment groups (210 mg/2 weeks, 405 mg/4 weeks, or 300 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 RELPREV-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 RELPREV and with incidence greater than placebo who participated in the 8-week, placebo-controlled trial.

#### Table 9: Treatment-Emergent Adverse Reactions

<table>
<thead>
<tr>
<th>Body System/Adverse Reaction</th>
<th>ZYPREXA RELPREV (N=100)</th>
<th>Placebo (N=98)</th>
<th>ZYPREXA RELPREV (N=106)</th>
<th>Placebo (N=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ear and Labyrinth Disorders</td>
<td>210 mg/2 wks</td>
<td>405 mg/4 wks</td>
<td>300 mg/2 wks</td>
<td></td>
</tr>
<tr>
<td>Ear pain</td>
<td>3</td>
<td>4</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal pain†</td>
<td>2</td>
<td>3</td>
<td>2</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>
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<td>4</td>
<td>3</td>
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<tr>
<td>Vomiting</td>
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<td>1</td>
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<td>General Disorders and</td>
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<td>Administration Site Conditions</td>
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<td>Infections and Infestations</td>
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<tr>
<td>Upper respiratory tract infection</td>
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<td>Viral infection</td>
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<td>Injury, Poisoning and</td>
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<tr>
<td>Procedural Complications</td>
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<td>Procedural pain</td>
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<td>Investigations</td>
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<td>Electrocardiogram QT-corrected interval prolonged</td>
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<td>0</td>
<td>2</td>
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<tr>
<td>Hepatic enzyme increased²</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Weight increased</td>
<td>5</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Metabolism and Nutrition Disorders</td>
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<td></td>
</tr>
<tr>
<td>Increased appetite</td>
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<td>1</td>
<td>4</td>
<td>6</td>
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<td>Musculoskeletal and</td>
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<td>Connective Tissue Disorders</td>
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<td>Arthralgia</td>
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<td>Back pain</td>
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<td>3</td>
<td>5</td>
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<td>Muscle spams</td>
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<td>2</td>
</tr>
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<td>Musculoskeletal stiffness</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td>4</td>
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<tr>
<td>Nervous System Disorders</td>
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<tr>
<td>Dizziness</td>
<td>2</td>
<td>4</td>
<td>4</td>
<td>1</td>
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<tr>
<td>Dysarthria</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
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<tr>
<td>Headache§</td>
<td>8</td>
<td>13</td>
<td>15</td>
<td>18</td>
</tr>
<tr>
<td>Somnolence</td>
<td>13</td>
<td>13</td>
<td>8</td>
<td>13</td>
</tr>
<tr>
<td>Tremor</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Psychiatric Disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal dreams</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Hallucination, auditory</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Restlessness</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Sleep disorder</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Thinking abnormal</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ZYPREXA RELPREV (olanzapine)</th>
<th>For Extended Release Injectable Suspension</th>
<th>ZYPR-0012-USPI-20210222</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZYPREXA RELPREV (olanzapine)</td>
<td>For Extended Release Injectable Suspension</td>
<td>ZYPR-0012-USPI-20210222</td>
</tr>
</tbody>
</table>
**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>ZYPREXA RELPREVV 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>
</tr>
</thead>
<tbody>
<tr>
<td>Reproductive System and Breast Disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal discharge</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Respiratory, Thoracic and Mediastinal Disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>5</td>
<td>3</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Nasal congestion</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Pharyngolaryngeal pain</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Sneezing</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Skin and Subcutaneous Tissue Disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acne</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Vascular Disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>0</td>
<td>3</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

- a The term abdominal pain upper was combined under abdominal pain.
- b The term tooth abscess was combined under tooth infection.
- c The terms alanine aminotransferase increased, aspartate aminotransferase increased, and gamma-glutamyltransferase increased were combined under hepatic enzyme increased.
- d The term tension headache was combined under headache.
- e The term somnolence was combined under sedation.
- f The term sinus congestion was combined under nasal congestion.

**Table 10: Treatment-Emergent 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</th>
<th>Olanzapine 5 ± 2.5 mg/day</th>
<th>Olanzapine 10 ± 2.5 mg/day</th>
<th>Olanzapine 15 ± 2.5 mg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parkinsonisma</td>
<td>15</td>
<td>14</td>
<td>12</td>
<td>14</td>
</tr>
<tr>
<td>Akathisiab</td>
<td>23</td>
<td>16</td>
<td>19</td>
<td>27</td>
</tr>
</tbody>
</table>

- a Percentage of patients with a Simpson-Angus Scale total score >3.
- b Percentage of patients with a Barnes Akathisia Scale global score ≥2.

**Table 11: Treatment-Emergent 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>Dystonic eventsa</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Parkinsonism eventsb</td>
<td>10</td>
<td>8</td>
<td>14</td>
<td>20</td>
</tr>
<tr>
<td>Akathisia eventsb</td>
<td>1</td>
<td>5</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Dyskinetic eventsb</td>
<td>4</td>
<td>0</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

- a Patients with the following COSTART terms were counted in this category: dystonia, generalized spasm, neck rigidity, oculogyric crisis, opisthotonus, torticollis.
- b Patients with the following COSTART terms were counted in this category: akinesia, cogwheel rigidity, extrapyramidal syndrome, hypertonia, hypokinesia, masked facies, tremor.
- c Patients with the following COSTART terms were counted in this category: akathisia, hyperkinesia.
- d Patients with the following COSTART terms were counted in this category: buccoglossal syndrome, choreoathetosis, dyskinesia, tardive dyskinesia.
- e Patients with the following COSTART terms were counted in this category: movement disorder, myoclonus, twitching.
Vital Signs and Laboratory Studies

Laboratory Changes

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

Statistically significant within group mean changes for ZYPREXA RELPREV, which were also significantly different from oral olanzapine (in a 24-week double-blind study), were observed for the following: gamma-glutamyltransferase (GGT) and sodium.

From an analysis of the laboratory data in an integrated database of 41 completed clinical studies in adult patients treated with oral olanzapine, high GGT levels were recorded in >1% (83/5245) of patients.

Statistically significant differences were observed between ZYPREXA RELPREV and oral olanzapine for the incidence of treatment-emergent low platelet count (0% ZYPREXA RELPREV vs 1% oral olanzapine; and ZYPREXA RELPREV vs 0.7% for oral olanzapine). There was a statistically significant difference between ZYPREXA RELPREV and oral olanzapine in potentially clinically significant changes for high leucocyte count (3% ZYPREXA RELPREV vs 1% oral olanzapine).

Changes inaminotransferases observed with ZYPREXA RELPREV treatment were similar to those reported with ZYPREXA treatment. In placebo-controlled ZYPREXA RELPREV studies, clinically significant ALT elevations (>3 times the upper limit of the normal range) were observed in 2.7% (8/291) of patients exposed to olanzapine compared to 3.2% (3/94) of the placebo group. None of these patients experienced jaundice. In 3 of these patients, liver enzymes reverted to the normal range despite continued treatment, and in 5 cases enzymes values decreased, but were still above the normal range at the end of therapy.

Within the larger premarketing ZYPREXA RELPREV database of 1586 patients with baseline ALT >30 U/L, the incidence of ALT elevations to >200 U/L was 0.8%. None of these patients experienced jaundice or other symptoms attributable to liver impairment and most had transient changes that tended to normalize while ZYPREXA RELPREV treatment was continued.

From an analysis of the laboratory data in an integrated database of 41 completed clinical studies in adult patients treated with oral olanzapine, elevated uric acid was recorded in >3% (171/4641) of patients.

Olanzapine Monotherapy in Adults: An assessment of the premarketing experience for oral olanzapine revealed an association with asymptomatic increases in ALT, AST, and GGT. Within the original integrated database of about 2400 adult patients with baseline ALT <30 U/L, the incidence of ALT elevations to >200 U/L was 2% (50/2531). None of these patients experienced jaundice or other symptoms attributable to liver impairment and most had transient changes that tended to normalize while treatment was continued.

In placebo-controlled olanzapine monotherapy studies in adults, clinically significant ALT elevations (change from <3 times the upper limit of normal [ULN] at baseline to ≥3 times ULN) were observed in 5% (77/1426) of patients exposed to olanzapine compared to 10% (1187) of patients exposed to placebo. ALT elevations >3 times ULN were observed in 2% (250/1426) of patients treated with olanzapine. ALT values returned to normal, or were decreasing, at last follow-up in the majority of patients who either continued treatment with olanzapine or discontinued olanzapine. No patient with elevated ALT values experienced jaundice, liver failure, or met the criteria for Hy’s Rule. Caution should be exercised in patients with signs and symptoms of hepatic impairment, in patients with pre-existing conditions associated with limited hepatic functional reserve, and in patients who are being treated with potentially hepatotoxic drugs.

Olanzapine administration was also associated with increases in serum prolactin [see Warnings and Precautions (5.13)].

ECG Changes — Comparison of ZYPREXA RELPREV and oral olanzapine, in a 24 week study, revealed no significant differences on ECG changes. Between-group comparisons for between-group comparisons for changes in aminotransferases observed with ZYPREXA RELPREV treatment were similar to those reported with ZYPREXA treatment. In placebo-controlled ZYPREXA RELPREV studies, clinically significant ALT elevations (>3 times the upper limit of normal range) were observed in 2.7% (8/291) of patients exposed to olanzapine compared to 3.2% (3/94) of the placebo group. None of these patients experienced jaundice. In 3 of these patients, liver enzymes reverted to the normal range despite continued treatment, and in 5 cases enzymes values decreased, but were still above the normal range at the end of therapy.

Pharmacokinetics

ZYPREXA RELPREV (olanzapine) is a racemic mixture. The mean peak plasma concentration occurred approximately 3-4 hours after administration. Absorption is complete with ZYPREXA RELPREV (olanzapine) and oral olanzapine.

There is a 50% increase in the clearance of olanzapine. This increase is likely due to the fact that carboxyzamide is a potent inducer of CYP1A2 activity. Higher daily doses of carboxyzamide may cause an even greater increase in olanzapine clearance.

Alcohol — Ethanol (45 mg/kg single dose) did not have an effect on olanzapine pharmacokinetics. The co-administration of alcohol (i.e., ethanol) with olanzapine potentiated the orthostatic hypotension observed with olanzapine [see Drug Interactions (7.3)].

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% and a decrease in AUC of 18%. Serotonergic smokers are at increased risk for this interaction. 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 modification is not routinely recommended.

Warfarin — Warfarin (20 mg single dose) did not affect olanzapine pharmacokinetics [see Drug Interactions (7.3)].

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

Anticholinergic Drugs — Concomitant treatment with olanzapine and other drugs with anticholinergic activity can increase the risk for severe gastrointestinal adverse reactions related to anticholinergic activity. ZYPREXA RELPREV should be used with caution in patients receiving medications having anticholinergic (antimuscarinic) effects [see Warnings and Precautions (5.16)].

7.2 Potential for Olanzapine to Affect Other Drugs

CNS Acting Drugs — Given the CNS effects of olanzapine, caution should be used when concomitant treatment 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 (M) — 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 somnolence observed with either drug given alone.

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.

Neuroleptics — 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.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to atypical antipsychotics, including ZYPREXA RELPREV, during pregnancy. Healthcare providers are encouraged to register patients by contacting the National Pregnancy Registry for Atypical Antipsychotics at 1-866-961-2388 or visit http://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/.

Risk Summary

Neonates exposed to antipsychotic drugs, including ZYPREXA RELPREV, during the third trimester at risk for extrapyramidal and/or withdrawal symptoms following delivery (see Clinical Considerations). Overall available data from published epidemiologic studies of pregnant women exposed to olanzapine have not established a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes (see Data). There are risks to the fetus associated with untreated schizophrenia or bipolar I disorder and with exposure to antipsychotics, including ZYPREXA RELPREV, during pregnancy (see Clinical Considerations). Olanzapine was not teratogenic when administered orally to pregnant rats and rabbits at doses that are 9-30 times the daily oral maximum recommended human dose (MRHD), based on mg/m2 body surface area; some fetal toxicities were observed at these doses (see Data). The estimated background risk of major birth defects and miscarriage for the indicated populations is unknown. All pregnancies have a background risk of birth defects, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Disease-associated maternal and embryo/fetal risk

There is a risk to the mother from untreated schizophrenia or bipolar I disorder, including increased risk of relapse, hospitalization, and suicide. Schizophrenia and bipolar I disorder are associated with increased adverse perinatal outcomes, including preterm birth. It is not known if this is a direct result of the illness or comorbid factors.

ZYPREXA RELPREV (olanzapine)

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ZYPREXA RELPREV (olanzapine)

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ZYPREXA RELPREV (olanzapine)
Fetal/Neonatal adverse reactions
Extrapyramidal and/or withdrawal symptoms, including agitation, hypotonia, hypoxia, tremor, somnolence, respiratory distress, and feeding disorder have been reported in neonates who were exposed to antipsychotic drugs, including ZYPREXA RELPREV, during the third trimester of pregnancy. Extrapyramidal and/or withdrawal symptoms were observed in several neonates for extrapyramidal and/or withdrawal symptoms and manage symptoms appropriately. Some neonates recovered within hours or days without specific treatment; others required prolonged hospitalization.

Data for Human Use
Placental passage has been reported in published study reports; however, the placental passage ratio was highly variable ranging between 7% to 167% at birth following exposure during pregnancy. The overall relevance of this finding is unknown.

Published data from observational studies, birth registry data, case reports and meta-analyses that have evaluated the use of atypical antipsychotics during pregnancy do not establish an increased risk of major birth defects. A retrospective cohort study from a Medicaid database of 9259 women exposed to antipsychotics during pregnancy did not indicate an overall increased risk for major birth defects.

Animal Data
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 daily oral MRHD based on mg/m² body surface area, 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 daily oral MRHD based on mg/m² body surface area), and gestation was prolonged at 10 mg/kg/day (5 times the daily oral MRHD based on mg/m² body surface area). In an oral rabbit teratology study, fetal toxicity manifested as increased resorptions and decreased fetal weight, occurred at a maternally toxic dose of 30 μg/kg/day (30 times the daily oral MRHD based on mg/m² body surface area). No evidence of teratogenicity or embryo-fetal toxicity was observed in rats or rabbits treated with olanzapine at intravenous and maintain an airway and 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 include cardiovascular monitoring should commence immediately and should include

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

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

11 DESCRIPTION
ZYPREXA RELPREV 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-methyl-1-piperazinyl)-,4,4´-methylenebis[3-hydroxy-2-naphthalenecarboxylate] (1:1), monohydrate. The formula is C₁₇H₂₂N₄S•C₂₃H₁₄O₆•H₂O, which corresponds to a molecular weight of 718.8.

The quantity of olanzapine in ZYPREXA RELPREV 2 mg for inj may be stated in terms of the amount of olanzapine olanzapine C₁₇H₂₂N₄S•C₂₃H₁₄O₆•H₂O. The content of olanzapine C₁₇H₂₂N₄S•C₂₃H₁₄O₆•H₂O is 99%, and the content of water is 1.0%.

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For Extended Release Injectable Suspension
ZYPRE-0012-USPI-20210222

ZYPREXA RELPREV (olanzapine)
ZYPR-0012-USPI-20210222_ZYPR-0002-MG-20191022_0080

ZYPREXA RELPREV, ZYPR-0012-USPI-20210222_ZYPR-0002-MG-20191022_0080

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ZYPREXA RELPREVV is a long-acting form of olanzapine and is intended for deep intramuscular gluteal injection only. ZYPREXA RELPREVV includes a single-dose vial of the drug product and a vial of the sterile diluent for ZYPREXA RELPREVV.

Mechanism of Action
The mechanism of action of olanzapine, in the listed indications is unclear. However, the efficacy of olanzapine in schizophrenia could be mediated through a combination of dopamine and serotonin type 2 (5HT2) antagonism.

Pharmacodynamics
Olanzapine binds with high affinity to the following receptors: serotonin 5HT2A/2C, 5HT6, histamine H1, dopamine D2, D4, and adrenergic α1 receptors. ZYPREXA RELPREVV is an antagonist with moderate affinity binding for serotonin 5HT2A, (Kd = 57nM) and muscarinic M1, M2, M3, M4, and M5 respectively. Olanzapine binds with low affinity to GABA_A, BZD, and β-adrenergic receptors (Kd > 10μM).

Pharmacokinetics
The fundamental pharmacokinetic properties of olanzapine are similar for 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 plasma concentrations that are sustained over a period of weeks to months. An injection every 2 or 4 weeks provides olanzapine concentrations that are comparable 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 concentration known to have been associated with efficacy in schizophrenia. Maximum 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 may not commonly be necessary.

Race — In vivo studies of orally administered olanzapine have shown that exposures are similar among Japanese, Chinese and Caucasians, especially after normalization for body weight. Dosing recommendations for race are, therefore, not necessary.

Combined Effects — The combined effects of age, smoking, and gender could lead to substantial pharmacokinetic differences in populations. The clearance in young smoking males, for example, may be 3 times higher than that in elderly nonsmoking females. Dosing modifications may therefore be necessary. For patients who have never taken ZYPREXA IntraMuscular are similar to those for orally administered olanzapine. Refer to the package insert for ZYPREXA IntraMuscular for additional information.

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 mg/kg/day (equivalent to 0.02–0.6 times the oral MRHD based on mg/m2 body surface area) and 100 mg/kg/day (equivalent to 16 times the oral MRHD based on mg/m2 body surface area). Rats were treated at doses of 0.25, 1, 2.5, 5, 10, and 20 mg/kg/day (equivalent to 0.06–2 times the daily oral MRHD based on mg/m2 body surface area). The incidence of liver hemangiosarcoma was significantly increased in 1 mouse study in female mice at 2 times the daily oral MRHD based on mg/m2 body surface area. These tumors were not increased in another mouse study in females dosed up to 2.5 times the daily oral MRHD based on mg/m2 body surface area, or in any other animal species at doses lower than the high dose used in the carcinogenicity study. The incidence of mammary gland adenomas and adenosarcomas 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 daily oral MRHD based on mg/m2 body surface area, respectively). Rats were also treated intramuscularly 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 daily oral MRHD of 300 mg every 2 weeks based on mg/m2 body surface area; dosing was limited due to local reactions at the IM injection site). The incidence of tumors in this study was lower than that observed for ZYPREXA RELPREVV control or pantoic acid treated animals. Antipsychotic drugs have been shown to chronically elevate prolactin levels in rodents. Serum prolactin levels were not measured during the olanzapine carcinogenicity studies; however, measurements during subchronic toxicity studies showed that olanzapine elevated serum prolactin levels in female rats at the same doses used in the carcinogenicity study. An increase in mammary gland neoplasms has been found in rodents after chronic administration of other antipsychotic drugs and is considered to be prolactin mediated. The relevance for human risk of the finding of prolactin mediated endocrine tumors in rodents is unknown (see Warnings and Precautions (2.17)).

Mutagenesis — There is no evidence of genotoxic potential for olanzapine was found in the Ames reverse mutation test, in vivo micronucleus test in mice, the chromosomal aberration test in Chinese hamster ovary cells, unscheduled DNA synthesis test in rat hepatocytes, induction of forward mutation test in mouse lymphoma cells, or in vivo sister chromatid exchange test in bone marrow of Chinese hamsters.

Impairment of Fertility — In an oral fertility and reproductive performance study in rats, male mating performance, but not fertility, was impaired at a dose of 22.4 mg/kg/day and female fertility was decreased at a dose of 3 mg/kg/day (11 and 1.5 times the daily oral MRHD based on mg/m2 body surface area, respectively). Discontinue of olanzapine treatment reversed the effects on male mating performance. In female rats, the precoital period was increased and the mating index reduced at 5 mg/kg/day (2.5 times the daily oral MRHD based on mg/m2 body surface area, respectively).
on mg/m² body surface area). Diestrous was prolonged and estrous delayed at 1.1 mg/kg/day (11 times the daily oral MRHD based on mg/m² body surface area) for 6 or 12 months. No evidence of bone marrow cytotoxicity was found in any of the species examined. Bone marrows were normocellular or hypocellular, indicating that the reductions in circulating blood cells were probably due to peripheral (non-marrow) factors.

14 CLINICAL STUDIES

14.1 Schizophrenia

The short-term effectiveness of ZYPREXA RELPREV was established in an 8-week, placebo-controlled trial in adult patients (n=1065) who were experiencing psychotic symptoms and met DSM-IV or DSM-IV-TR criteria for schizophrenia. Patients were randomized to receive injections of ZYPREXA RELPREV 210 mg every 2 weeks, ZYPREXA RELPREV 405 mg every 4 weeks, ZYPREXA RELPREV 300 mg every 2 weeks, or placebo every 2 weeks. Patients were discontinued from their previous antipsychotics and underwent a 2-7 day washout period. No oral antipsychotic supplementation was allowed throughout the trial. The primary efficacy measure was change from baseline to endpoint in Positive and Negative Syndrome Scale (PANSS) score (mean baseline total PANSS score 56) and were then randomized to continue their current oral olanzapine doses (10, 15, or 20 mg/day), or to ZYPREXA RELPREV 150 mg every 2 weeks (405 mg every 4 weeks, 300 mg every 2 weeks, or 45 mg every 4 weeks). No oral antipsychotic supplementation was allowed throughout the trial. The primary efficacy measure was time to exacerbation of symptoms of schizophrenia defined in terms of increases in Brief Psychiatric Rating Scale (BPRS) positive symptoms or hospitalization. ZYPREXA RELPREV doses of 150 mg every 2 weeks, 405 mg every 4 weeks, and 300 mg every 2 weeks were each statistically significantly superior to low dose ZYPREXA RELPREV (45 mg every 4 weeks).

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

ZYPREXA RELPREV convenience kit is supplied in single dose cartons. Each carton includes one vial of olanzapine pamoate monohydrate in dosage strengths that are equivalent to 210 mg olanzapine (483 mg olanzapine pamoate monohydrate), 300 mg olanzapine (690 mg olanzapine pamoate monohydrate), and 405 mg olanzapine (931 mg olanzapine pamoate monohydrate) per vial; one vial of approximately 3 mL of diluent for ZYPREXA RELPREV used to suspend the drug product, one 3-mL syringe with pre-filled 19-gauge 1-inch Hypodermic Needle-Pro needle with needle protection device, and two 19-gauge, 1.5-inch (38 mm) Hypodermic Needle-Pro needles with needle protection device.

Needle-Pro® is a registered trademark of Smiths Medical.

NDC 002-7636-11 — single-dose convenience kit: 210 mg vial (VL7635) with rust flip-off cap and 3-mL vial of sterile diluent (VL7622) with gray flip-off cap

NDC 002-7636-11 — single-dose convenience kit: 300 mg vial (VL7636) with olive flip-off cap and 3-mL vial of sterile diluent (VL7622) with gray flip-off cap

NDC 002-7636-11 — single-dose convenience kit: 405 mg vial (VL7637) with steel blue flip-off cap and 3-mL vial of sterile diluent (VL7622) with gray flip-off cap

16.2 Storage and Handling

ZYPREXA RELPREV should be stored at room temperature not to exceed 30°C (86°F). When the drug product is suspended in the solution for ZYPREXA RELPREV, it may be held at room temperature for 24 hours. The vial should be agitated immediately prior to product withdrawal. Once the suspension is withdrawn into the syringe, it should be used immediately [see Dosage and Administration (2.2)].

17 PATIENT COUNSELING INFORMATION

Advisement

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Patients should be advised of the following issues and asked to alert their prescriber if these occur while taking ZYPREXA RELPREV. Patients should be advised to call their doctor if they do not think they are getting better or have concerns about their condition.

Post-Injection Delirium/Sedation Syndrome

During marketing clinical studies, reactions that presented with signs and symptoms consistent with delirium overdose have been reported in patients following an injection of ZYPREXA RELPREV. It is mandatory that patients be enrolled in the ZYPREXA RELPREV Patient Care Program to receive ZYPREXA RELPREV treatment. Patients should be advised of the risk of post-injection delirium/sedation syndrome each time they receive an injection [see Warnings and Precautions (5.1, 5.2)]. Patient and caregivers should be advised that after each ZYPREXA RELPREV injection, patients must be observed at the healthcare facility for at least 3 hours and must be accompanied to their destination upon leaving the facility. The Medication Guide should be distributed each time patients receive an injection.

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

ZYPREXA RELPREV (olanzapine) For Extended Release Injectable Suspension ZYPRE-0012-USPI-20210222

ZYPREXA RELPREV (olanzapine) For Extended Release Injectable Suspension ZYPRE-0012-USPI-20210222
Medication Guide
ZYPREXA® RELPREVV™ (zy-PREX-a REL-prev)
(olanzapine)
For Extended Release Injectable Suspension

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)
Serious side effects may happen when you take ZYPREXA RELPREVV, For Extended Release Injectable Suspension ZYPREXA RELPREVV (olanzapine) 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 prescription and nonprescription medicines, vitamins, and herbal including Tell your doctor about all the medicines that you take, doctor or go to an emergency room right away.

The symptoms of schizophrenia may include thoughts of suicide or hurting yourself or any other medical condition are pregnant or plan to become pregnant. If it is not known if ZYPREXA RELPREVV will harm your unborn baby.
- If you become pregnant while receiving ZYPREXA, talk to your healthcare provider about registering with the National Pregnancy Registry for Atypical Antipsychotics. You can register by calling 1-866-961-2388 or go to http://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/.
- are breast-feeding or plan to breast-feed. ZYPREXA RELPREVV passes into your breast milk. 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.

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www.zyprexarelprevv.com

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ZYPREXA RELPREVV (olanzapine)
For Extended Release Injectable Suspension ZYPR-0002-MG-20191022

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