

## Olanzapine Pamote

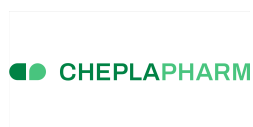
## Developer(s)

CHEPLAPHARM

Originator

<https://www.cheplapharm.com/en/>

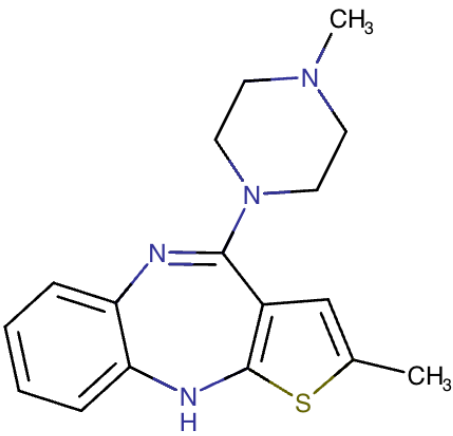
Germany



Cheplapharm Arzneimittel GmbH is a pharmaceutical company headquartered in Greifswald, Germany. In 2023, they acquired the worldwide commercial rights for Zyprexa® from Eli Lilly and Company. This portfolio included olanzapine formulations marketed under the brand names ZypAdhera® and ZYPREXA® RELPREVV™. These products are indicated for the treatment of schizophrenia and bipolar disorders.

Cheplapharma

## Drug structure


$$\text{H}_2\text{O}$$

## Olanzapine Pamoate Chemical Structure

Sourced from DrugBank

# Drug information

## Associated long-acting platforms

Crystalline salt depot, Aqueous drug particle suspension

## Administration route

Oral, Intramuscular

## Therapeutic area(s)

Mental health

## Use case(s)

Treatment

## Use of drug

### Ease of administration

Administered by a nurse

Administered by a specialty health worker

### User acceptance

Not provided

## Dosage

### Available dose and strength

Not provided

### Frequency of administration

Not provided

### Maximum dose

Not provided

### Recommended dosing regimen

Not provided

### Additional comments

Not provided

### Dosage link(s)

Not provided

## Drug information

### Drug's link(s)

Not provided

### Generic name

Olanzapine pamoate

### Brand name

ZypAdhera®, ZYPREXA® RELPREVV™.

### Compound type

Small molecule

### Summary

Olanzapine is a second generation antipsychotic used for the treatment of schizophrenia and bipolar disorder. Long-acting injectable olanzapine formulations utilise a crystalline salt comprised of olanzapine and pamoic acid that forms micron-sized crystals in aqueous suspension. After administration via deep intramuscular injection, olanzapine pamoate forms a depot that gradually dissolves over a time period of approximately four weeks, with an average half-life of 30 days. The distribution and absorption of olanzapine pamoate occurs quickly and it remains in systemic circulation for 6-8 months following the last injection. 93% of olanzapine pamoate is bound to  $\alpha$ 1-acid-glycoprotein and albumin. Smoking may reduce the effectiveness of olanzapine, as it is metabolised by the CYP1A2 enzyme.

### Approval status

Unknown

### Regulatory authorities

Unknown

**Delivery device(s)**

No delivery device

# **Scale-up and manufacturing prospects**

## **Scale-up prospects**

Compound is commercially manufactured.

## **Tentative equipment list for manufacturing**

Not provided

## **Manufacturing**

The manufacturing process includes media conditioning, compounding, particle size reduction, vial filling, lyophilisation, and terminal sterilisation to produce a sterile injectable formulation. Olanzapine particles are reduced to <600 nm (preferably <100 nm) using nano-milling, homogenisation, or precipitation. Spherical grinding media (beads ~0.01mm to 3 mm) made of polymeric resin, glass or Zirconium Silicate are used. Olanzapine is mixed with liquid to form a premix (5-60% concentration) and surface stabiliser is added. The pH of the liquid dispersion is maintained between 3.0 and 8.0.

## **Specific analytical instrument required for characterization of formulation**

Horiba LA 910 particle size analyser.

# Clinical trials

**TV44749-PK-10188**

## Identifier

NCT06253546

## Link

<https://clinicaltrials.gov/study/NCT06253546>

## Phase

Phase I

## Status

Recruiting

## Sponsor

Teva Branded Pharmaceutical Products R&D, Inc.

## More details

Primary Objective: To evaluate the safety and tolerability of single doses of TV-44749 for subcutaneous (sc) use in Chinese participants with schizophrenia. Secondary Objectives: \* To evaluate the pharmacokinetics (PK) of single doses of TV-44749 administered sc. \* To evaluate the pharmacokinetics of oral olanzapine tablets following multiple dose administration. \* To monitor the safety and tolerability of multiple doses of oral olanzapine tablets given in the study.

## Purpose

# Safety, Tolerability, and Pharmacokinetic Study of TV-44749 in Chinese Patients With Schizophrenia

## Interventions

### Intervention 1

Drug: TV-44749

### Intervention 2

Drug: Oral Olanzapine (ZYPREXA)

## Countries

China

## Sites / Institutions

Not provided

## Trials dates

### Anticipated Start Date

Not provided

### Actual Start Date

2024-03-28

### Anticipated Date of Last Follow-up

2024-05-08

### Estimated Primary Completion Date

2025-01-31

### Estimated Completion Date

2025-01-31

### Actual Primary Completion Date

Not provided

**Actual Completion Date**

Not provided

**Studied populations****Age Cohort**

- Adults

**Genders**

- All

**Accepts pregnant individuals**

No

**Accepts lactating individuals**

Unspecified

**Accepts healthy individuals**

No

**Comments about the studied populations**

Inclusion Criteria: - Body weight >50 kg and BMI between 18.5-38.0 kg/m<sup>2</sup>, inclusive, at the time of screening. - Current diagnosis of schizophrenia according to evaluation by the investigator, using DSM-5. - Clinically stable, on oral olanzapine (i.e., dose has not changed in the last 4 weeks), and not currently on other antipsychotic treatment at the time of screening. - No hospitalization for worsening of schizophrenic symptoms and no significant exacerbation of schizophrenic symptoms within the 3 months prior to screening. - Participants must be surgically sterile or use an approved method of birth control. - Have no ongoing or expected significant life events. - Agree to maintain current smoking or nonsmoking status.

**Health status**

Not provided

**Study type**

Interventional (clinical trial)

**Enrollment**

36

**Allocation**

Non-randomized

**Intervention model**

Parallel Assignment

**Intervention model description**

Not provided

**Masking**

Open label

**Masking description**

None (Open Label)

**Frequency of administration**

Other : "Single dose "

**Studied LA-formulation(s)**

Injectable

**Studied route(s) of administration**

Subcutaneous

**Use case**

Treatment

## **Key resources**

Not provided

6390

## Identifier

NCT00320489

## Link

<https://clinicaltrials.gov/study/NCT00320489>

## Phase

Phase III

## Status

Completed

## Sponsor

Eli Lilly and Company

## More details

To compare the health outcome of patients with schizophrenia, who are at risk for relapse, when treated with a long acting injection form of olanzapine versus treatment with oral olanzapine.

## Purpose

Olanzapine Pamoate Depot Versus Oral Olanzapine on Treatment Outcomes in Outpatients With Schizophrenia

## Interventions

### Intervention 1

Drug: Olanzapine pamoate depot

Dosage: 150-405 mg

## **Intervention 2**

Drug: Olanzapine oral tablets

Dosage: 5-20 mg

## **Countries**

Argentina

Brazil

Canada

France

Greece

Portugal

Puerto Rico

Romania

Slovakia

Spain

Taiwan, Province of China

United States of America

## **Sites / Institutions**

Not provided

## **Trials dates**

### **Anticipated Start Date**

Not provided

### **Actual Start Date**

2006-04-01

### **Anticipated Date of Last Follow-up**

2012-01-19

### **Estimated Primary Completion Date**

Not provided

**Estimated Completion Date**

Not provided

**Actual Primary Completion Date**

2009-09-01

**Actual Completion Date**

2009-09-01

**Studied populations**

**Age Cohort**

- Adults
- Older Adults

**Genders**

- All

**Accepts pregnant individuals**

No

**Accepts lactating individuals**

No

**Accepts healthy individuals**

No

**Comments about the studied populations**

Inclusion Criteria: - Clinical diagnosis of schizophrenia. - Must be an outpatient (not requiring hospitalization) now and for at least the past 8 weeks. - Disease symptoms must meet a certain range as assessed by the clinician. - Patient has experienced at least two episodes of clinical worsening of their condition. This could mean admission to a hospital or an emergency room visit. This could mean that a new medication was

added, medication dose was increased, or medication was switched in order to better control symptoms of the condition. - The patient must have an unsatisfactory response to their current medication or be experiencing negative effects of their current medication or not always take their current medication so that a change in current medication is desired.

## **Health status**

Not provided

## **Study type**

Interventional (clinical trial)

## **Enrollment**

524

## **Allocation**

Randomized

## **Intervention model**

Parallel Assignment

## **Intervention model description**

Not provided

## **Masking**

Open label

## **Masking description**

None (Open Label)

## **Frequency of administration**

Monthly

### **Studied LA-formulation(s)**

Injectable

### **Studied route(s) of administration**

Intramuscular

### **Use case**

Treatment

### **Key resources**

Not provided

# TV44749-NPC-10205

## Identifier

NCT06319170

## Link

<https://clinicaltrials.gov/study/NCT06319170>

## Phase

Phase I

## Status

Recruiting

## Sponsor

Teva Branded Pharmaceutical Products R&D, Inc.

## More details

The primary objective of the study is to characterize the pharmacokinetics of 3 formulations of olanzapine. A secondary objective is to evaluate the safety and tolerability of 3 formulations of olanzapine. Another secondary objective is to characterize the pharmacokinetics of ZYPREXA. The planned duration of the study for each participant is 19 weeks.

## Purpose

Open-label Trial Characterizing the PK of 3 SC Olanzapine Extended-release Formulations in Participants With Schizophrenia/Schizoaffective Disorder

## Interventions

### Intervention 1

Drug: Olanzapine Extended Release

## Countries

United States of America

## Sites / Institutions

Not provided

## Trials dates

### Anticipated Start Date

Not provided

### Actual Start Date

2024-03-28

### Anticipated Date of Last Follow-up

2024-06-11

### Estimated Primary Completion Date

2024-12-11

### Estimated Completion Date

2024-12-11

### Actual Primary Completion Date

Not provided

### Actual Completion Date

Not provided

## Studied populations

### Age Cohort

- Adults

## **Genders**

- All

## **Accepts pregnant individuals**

No

## **Accepts lactating individuals**

No

## **Accepts healthy individuals**

No

## **Comments about the studied populations**

Inclusion Criteria: - Body weight >50 kg and body mass index (BMI) within the range 18.5 to 38.0 kg/m<sup>2</sup>, inclusive, at the time of screening. - Agree to maintain current smoking or nonsmoking status at the time informed consent is obtained and throughout the trial until completion of the end of treatment or early termination (ET) visit (ie, nonsmoking participants must agree not to start smoking and participants who smoke will be excluded if they plan to discontinue smoking during the trial. - Agree to the inpatient periods required during the trial period - Have a current confirmed diagnosis of schizophrenia or schizoaffective disorder according to an evaluation by the Investigator, using DSM-5. - Have no ongoing or expected significant life events.

## **Health status**

Not provided

## **Study type**

Interventional (clinical trial)

## **Enrollment**

95

## **Allocation**

Randomized

## **Intervention model**

Parallel Assignment

## **Intervention model description**

Not provided

## **Masking**

Open label

## **Masking description**

None (Open Label)

## **Frequency of administration**

Other : "Single dose "

## **Studied LA-formulation(s)**

Injectable

## **Studied route(s) of administration**

Subcutaneous

## **Use case**

Treatment

## **Key resources**

Not provided

5995

## Identifier

NCT00088465

## Link

<https://clinicaltrials.gov/study/NCT00088465>

## Phase

Phase III

## Status

Completed

## Sponsor

Eli Lilly and Company

## More details

This is a long-term, open-label clinical study designed to enable longer-term treatment of patients completing other clinical studies with intramuscular olanzapine depot. Key objectives of the study are to: \* Determine how well intramuscular (IM) olanzapine depot works during long-term treatment, \* Evaluate the safety and tolerability of IM olanzapine depot during long-term treatment, \* Determine the blood levels of IM olanzapine depot in patients during long-term treatment

## Purpose

Open-Label Study of Intramuscular Olanzapine Depot in Patients With Schizophrenia or Schizoaffective Disorder

## Interventions

## **Intervention 1**

Drug: Intramuscular olanzapine depot (Zyprexa Adhera)

Dosage: 45-405 mg

## **Countries**

Argentina

Australia

Austria

Belgium

Brazil

Czechia

Croatia

France

Germany

Hungary

Israel

Italy

Mexico

Netherlands

Poland

Portugal

Puerto Rico

Romania

Russian Federation

Slovakia

South Africa

Spain

Sweden

Taiwan, Province of China

United States of America

## **Sites / Institutions**

Not provided

## **Trials dates**

### **Anticipated Start Date**

Not provided

### **Actual Start Date**

2004-08-01

### **Anticipated Date of Last Follow-up**

2011-12-09

### **Estimated Primary Completion Date**

Not provided

### **Estimated Completion Date**

Not provided

### **Actual Primary Completion Date**

2010-12-01

### **Actual Completion Date**

2010-12-01

## **Studied populations**

### **Age Cohort**

- Adults
- Older Adults

### **Genders**

- All

### **Accepts pregnant individuals**

No

### **Accepts lactating individuals**

No

### **Accepts healthy individuals**

No

### **Comments about the studied populations**

Inclusion Criteria: - Patients must have schizophrenia. - Female patients of childbearing potential must be using a medically accepted means of contraception. - Patients must have completed (within 10 days) another IM olanzapine depot study if permitted by that study's protocol. Exclusion Criteria: - Patients must not have participated in a clinical trial of another investigational drug, including olanzapine, within 1 month (30 days) prior to study entry. - Female patients must not be pregnant or breast-feeding. - Patients must not be experiencing acute, serious or unstable medical conditions other than schizophrenia or schizoaffective disorder. - Patients must not have a substance (except nicotine or caffeine) dependence within the past 30 days.

### **Health status**

Not provided

### **Study type**

Interventional (clinical trial)

### **Enrollment**

931

### **Allocation**

Non-randomized

### **Intervention model**

Single group assignment

### **Intervention model description**

Not provided

## Masking

Open label

## Masking description

None (Open Label)

## Frequency of administration

Other : "2-, 3-, or 4-week interval. "

## Studied LA-formulation(s)

Injectable

## Studied route(s) of administration

Intramuscular

## Use case

Treatment

## Key resources

Type	Title	Content	Link
Link	Long-term safety and efficacy of olanzapine long-acting injection in patients with schizophrenia or schizoaffective disorder: a 6-year, multinational, single-arm, open-label study		<a href="https://doi.org/10.1097/yic.0000000000000000">https://doi.org/10.1097/yic.0000000000000000</a>



# Excipients

## **Proprietary excipients used**

Not provided

## **Novel excipients or existing excipients at a concentration above Inactive Ingredients Database (IID) for the specified route of administration**

Not provided

## **Residual solvents used**

Not provided

## Patent info

There are either no relevant patents or these were not yet submitted to LAPaL

# Supporting material

## Publications

Samalin L, Garay R, Ameg A, Llorca PM. Olanzapine pamoate for the treatment of schizophrenia--a safety evaluation. *Expert Opin Drug Saf*. 2016;15(3):403-11. DOI: 10.1517/14740338.2016.1141893. Epub 2016 Feb 19. PMID: 26761429.

**Introduction:** Non-adherence to long-term treatment is a major issue for patients with schizophrenia and is associated with an increased risk of relapse. Long-acting injectable (LAI) antipsychotics can offer a useful option to improve adherence. Due to the type of sustained-release mechanism, olanzapine pamoate (OLAI) can differ in safety as compared with oral olanzapine. Recent safety data concerning olanzapine pamoate required an update of previous systematic reviews.

**Areas covered:** Safety data were found in US and EU clinical trial registries, and a literature search was undertaken using the databases PubMed and EMBASE to find all relevant published studies. Where appropriate, the number needed to harm and 95% confidence interval for categorical safety outcomes were calculated.

**Expert opinion:** The safety profile of OLAI was similar to the well-known safety profile of oral olanzapine, except for the risk of occurrence of post-injection delirium/sedation syndrome (PDSS). Olanzapine pamoate can be a choice for schizophrenic patients with a history of response to and acceptable tolerance of oral olanzapine, who have easy access to mental healthcare settings with emergency services for the treatment of PDSS. Long-term, prospective studies assessing the efficacy and safety of OLAI and head-to-head comparisons with other LAI and oral antipsychotics are needed.

## Additional documents

No documents were uploaded

## Useful links

- [Long-term safety and efficacy of olanzapine long-acting injection in patients with schizophrenia or schizoaffective disorder: a 6-year, multinational, single-arm, open-label study](#)

# Access principles

## Collaborate for development



Consider on a case by case basis, collaborating on developing long acting products with potential significant public health impact, especially for low- and middle-income countries (LMICs), utilising the referred to long-acting technology

Not provided

## Share technical information for match-making assessment



Provide necessary technical information to a potential partner, under confidentiality agreement, to enable preliminary assessment of whether specific medicines of public health importance in LMICs might be compatible with the referred to long-acting technology to achieve a public health benefit

Not provided

## Work with MPP to expand access in LMICs



In the event that a product using the referred to long-acting technology is successfully developed, the technology IP holder(s) will work with the Medicines Patent Pool towards putting in place the most appropriate strategy for timely and affordable access in low and middle-income countries, including through licensing

Not provided

## Comment & Information

Not provided