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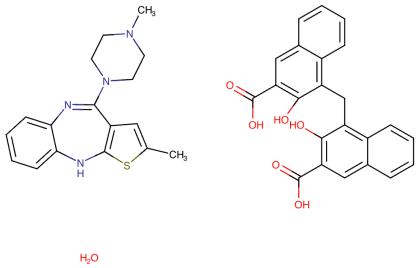


Olanzapine Pamoate

Developer(s)

CHEPLAPHARM

Originator

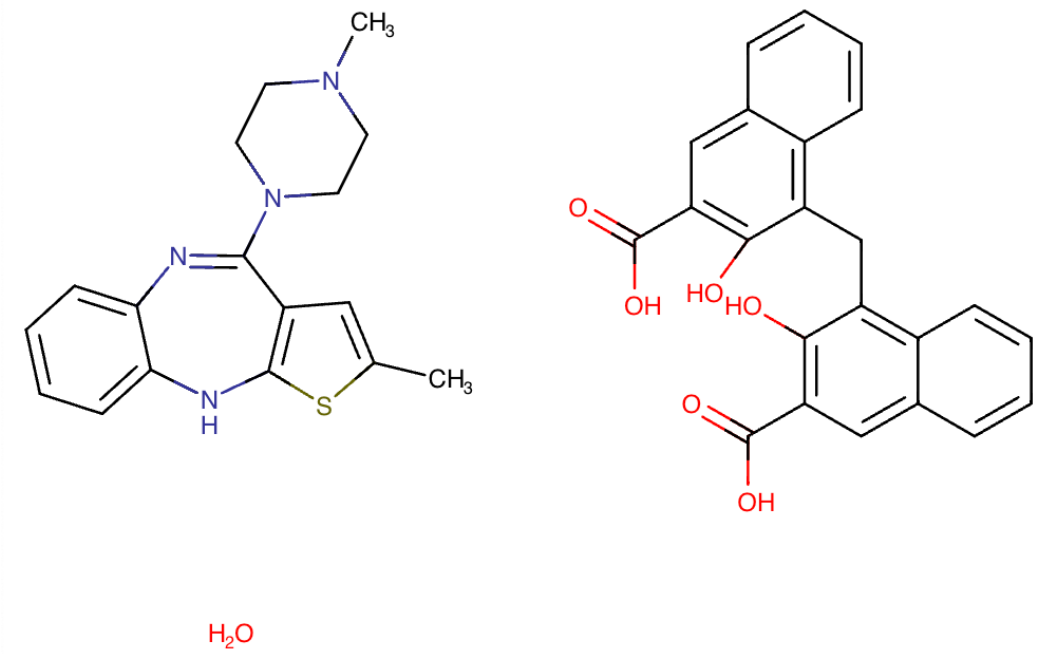
https://www.cheplapharm.com/en/

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



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 α1-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/m2, 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/m2, 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		https://doi.org/10.1097/yic.0

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