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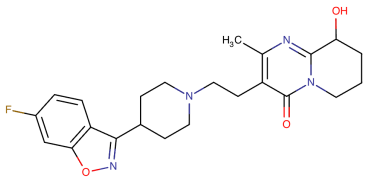


Paliperidone Palmitate Six-Monthly (PP6M)

Developer(s)

Janssen Pharmaceuticals

Originator

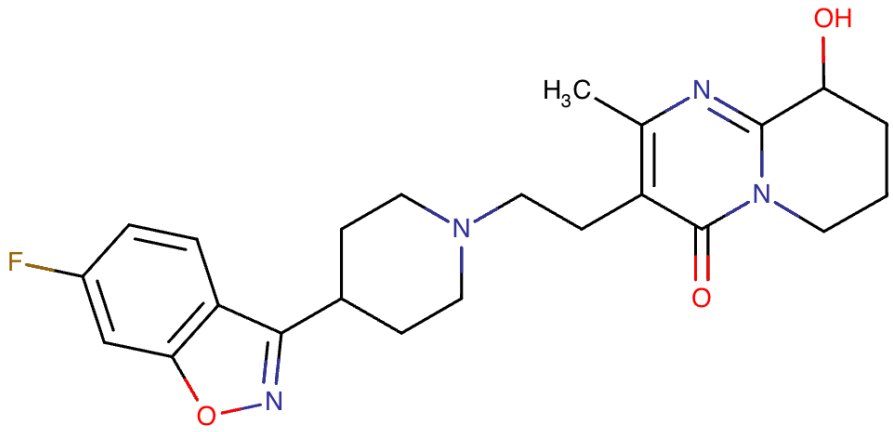
https://www.janssen.com/

Belgium

Janssen Pharmaceuticals is a subsidiary company of Johnson & Johnson headquartered in Beerse, Belgium. They focus on manufacturing and developing pharmaceutical products for use in areas such as, Immunology, Infectious Diseases & Vaccines, Pulmonary Hypertension, Cardiovascular & Metabolism, Oncology, and Neuroscience.

Janseen Cilag Pharmaceuticals

Drug structure



Paliperidone Compound Structure

Sourced From Drugbank

Drug information

Associated long-acting platforms

Aqueous drug particle suspension, Nanocrystal technology

Administration route

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

Paliperidone Palmitate Six-Monthly (PP6M)

Brand name

INVEGA HAFYERA®, BYANNLI®

Compound type

Small molecule

Summary

Paliperidone palmitate administered as a once every six-month long-acting injectable (PP6M) is indicated for the maintenance treatment of schizophrenia in adult patients who are adequately treated with 1-monthly paliperidone palmitate injection at doses of 100 mg or 150 mg (preferably for four months or more) or 3-monthly paliperidone palmitate injection at doses of 350 mg or 525 mg (for at least one injection cycle) and do not require dose adjustment. BYANNLI® and INVEGA HAFYERA® manufactured by Janssen Pharmaceuticals are available in dosage formulations of 700mg and 1000mg. Maximum plasma concentrations of PP6M are achieved after approx. 33-35 days (median Tmax), and are expected to remain in circulation for up to four years at < 1% of the average steady state levels.

Approval status

PP6M was approved under the trade name of INVEGA HAFYERA® in August 2021 by the United States Food and Drug Administration (US FDA) for the treatment of schizophrenia in patients after they have been adequately treated with INVEGA

SUSTENNA® (PP1M) for at least 4 months OR an every-three-month paliperidone palmitate (PP3M) extended-release injectable suspension (e.g., INVEGA TRINZA®) for at least one three-month cycle. PP6M is also approved by the European Medicines Agency (EMA) under the trade name of BYANNLI® (previously Paliperidone Janssen) for the maintenance treatment of schizophrenia in adult patients who are clinically stable on PP1M or PP3M. The transition to BYANNLI should be initiated in place of the next scheduled dose of paliperidone palmitate injection.

Regulatory authorities

PP6M (1000 mL/5 mL and 750 mg/3.5 mL) has received regulatory approval from 15 Drug Regulatory Authorities across 45 countries, including the FDA, EMA, TGA, MEDSAFE, DH, KMFDS, HSA, NPRA, ISP, INVIMA, Rwanda FDA, SFDA, ALIMS, NMPA, and DCH. The formulation is marketed under the brand name BYANNLI in the European Union (EU) and European Economic Area (EEA). In other regions, including the United States, Australia, New Zealand, Hong Kong, South Korea, Singapore, Malaysia, Chile, Colombia, China, Thailand, and Georgia, it is branded as INVEGA HAYFERA.

Delivery device(s)

No delivery device

Scale-up and manufacturing prospects

Scale-up prospects

PP6M is commercially manufactured by Janssen Pharmaceuticals. The PP6M injectable contains a racemic mixture of (+)- and (-)- of paliperidone, and is joined with palmitic acid through an ester linkage. Similarly to paliperidone palmitate once-monthly injectable (PP1M) and three-monthly injectable (PP3M), PP6M is manufactured using Nanocrystal Technology to improve the dissolution properties of paliperidone palmitate, which is highly insoluble in water. PP6M has a bi-annual dosing interval arising from a higher concentration and an increased nanocrystal particle size.

Tentative equipment list for manufacturing

NanoCrystal® Colloidal Dispersion Nanomill™ apparatus.

Manufacturing

NanoCrystal technology enables intrinsically high loading of insoluble drugs as dosage forms consist mostly of pure API packed as a solid crystal, which is the most efficient form possible in relation to weight-to-volume. Paliperidone palmitate particles are dispersed in an aqueous suspension and transformed into smaller nanocrystals through particle-size reduction. These nanocrystals have a greater surface area than the larger original particles, resulting in increased water solubility. This medicinal product does not require any special storage conditions and has a shelf life of two years.

Specific analytical instrument required for characterization of formulation

Digital microscope and scanning electron microscopy (SEM) to determine shape of the particles. Differential scanning calorimetric (DSC) and Fourier transforms infrared spectroscopy (FTIR) for quality control.

Clinical trials

CR108605

Identifier

NCT04072575

Link

https://clinicaltrials.gov/study/NCT04072575

Phase

Phase III

Status

Completed

Sponsor

Janssen Research & Development, LLC

More details

The main purpose of this study is to assess the long-term safety and tolerability of paliperidone 6-month PP6M (Dose 1 or Dose 2 \[milligram\] mg eq.) and to provide access to PP6M in participants with schizophrenia completing the R092670PSY3015 study without relapse.

Purpose

A Study of Paliperidone Palmitate 6-Month Formulation

Interventions

Intervention 1

Drug: Paliperidone Palmitate 6 month (PP6M)

Dosage: 700mg or 1000mg

Countries

Argentina

Hong Kong

Italy

Poland

Russian Federation

Ukraine

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2019-09-19

Anticipated Date of Last Follow-up

2023-05-03

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2022-05-03

Actual Completion Date

2022-05-03

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: - Completed the Double-blind Phase of Study R092670PSY3015 without relapse and continue to be willing to be treated with paliperidone palmitate 6 month injection (PP6M). - Must, in the opinion of the investigator, be able to continue treatment at the same dose level (moderate or higher dose) as used during the Double-blind Phase of Study R092670PSY3015 at the time of screening for this study. - A woman of childbearing potential: a) Must have a negative pregnancy test on Day 1; b) Use contraception consistent with local regulations. A man must agree that during the study and for a minimum 12 months after receiving the last dose of the study intervention: a) His female partner(s) will use highly effective method pf contraception. - Signed an informed consent form (ICF).

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

178

Allocation

Not provided

Intervention model

Single group assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Once every 6 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intramuscular

Use case

Treatment

Key results

Not provided

CR108390

Identifier

NCT03345342

Link

https://clinicaltrials.gov/study/NCT03345342

Phase

Phase III

Status

Completed

Sponsor

Janssen Research & Development, LLC

More details

The purpose of this study is to demonstrate that injection cycles consisting of a single administration of paliperidone palmitate 6-month (PP6M) are not less effective than 2 sequentially administered injections of paliperidone palmitate 3-month PP3M) (350 or 525 mg eq.) for the prevention of relapse in participants with schizophrenia previously stabilized on corresponding doses of paliperidone palmitate 1-month (PP1M) (100 or 150 mg eq.) or PP3M (350 or 525 mg eq.).

Purpose

A Study of Paliperidone Palmitate 6-Month Formulation

Interventions

Intervention 1

Drug: PP6M

Dosage: 700mg or 1000mg

Intervention 2

Drug: PP3M

Dosage: 350 mg eq. or 525 mg eq.

Intervention 3

Drug: PP1M

Dosage: 50mg to 150 mg eq.

Intervention 4

Other: Placebo

Dosage: 0 mg

Countries

Argentina

Australia

Brazil

Bulgaria

Czechia

France

Hong Kong

Hungary

India

Italy

Korea, Republic of

Malaysia

Mexico

Poland

Russian Federation

South Africa

Spain

Taiwan, Province of China

Türkiye

Ukraine

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2017-11-20

Anticipated Date of Last Follow-up

2023-09-13

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2020-05-08

Actual Completion Date

2020-05-08

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: - Must meet the diagnostic criteria for schizophrenia according to Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM 5) for at least 6 months before screening. - Must be receiving treatment with paliperidone palmitate (as either the paliperidone palmitate 1-month (PP1M) or paliperidone palmitate 3-month (PP3M) formulation), or injectable risperidone, or any oral antipsychotic. - Must be able, in the opinion of the investigator, to discontinue any antipsychotic medication other than PP1M) or PP3M during the Screening Phase. - Must have a full Positive and Negative Syndrome Scale (PANSS) score of less than (\<) 70 points at screening. - Must have a body mass index (BMI) between 17 and 40 kilogram (kg)/meter (m)\^2 (inclusive).

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

841

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Double-blind masking

Masking description

Double (Participant, Investigator).

Frequency of administration

Once every 6 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intramuscular

Use case

Treatment

Key results

Type of key results	Title	Website link

Article	A Randomized, Double-Blind, Multicenter, Noninferiority Study Comparing Paliperidone Palmitate 6-Month Versus the 3-Month Long-Acting Injectable in Patients With Schizophrenia	https://doi.org/10.1093/ijnp/pyab071

Excipients

Proprietary excipients used

No proprietary excipient used

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

No novel excipient or existing excipient used

Residual solvents used

No residual solvent used

Patent info

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

Supporting material

Publications

Peters L, Dyer M, Schroeder E, D'Souza MS. Invega Hafyera (Paliperidone Palmitate): Extended-Release Injectable Suspension for Patients With Schizophrenia. J Pharm Technol. 2023 Apr;39(2):88-94. DOI: 10.1177/87551225231153541. Epub 2023 Mar 16. PMID: 37051282; PMCID: PMC10084407.

Objective: The objective of this study was to describe the safety, efficacy, and potential role in therapy of once in 6 months paliperidone palmitate formulation (PP6M; Invega Hafyera). PP6M is a long-acting injectable antipsychotic recently approved by the Food and Drug Administration (FDA) for the treatment of schizophrenia. **Data Sources:** A PubMed literature search was conducted using the following terms: paliperidone palmitate and long-acting antipsychotic injections (January 1, 2017, to November 1, 2022). FDA product labeling was also reviewed for pertinent data. **Study Selection and Data Extraction:** All relevant English-language articles focused on the efficacy and safety of PP6M were considered for inclusion. **Data Synthesis:** A multicenter, randomized, active controlled relapse prevention noninferiority study showed that PP6M is comparable to paliperidone palmitate once in 3 months formulation (PP3M) in terms of efficacy and safety in clinically stable schizophrenia patients. **Place in Therapy:** PP6M is indicated in the treatment of adult patients with schizophrenia, who need treatment over a prolonged period. It improves adherence and decreases the rate of relapse and hospitalizations among patients with schizophrenia. It is useful for patients who may have difficulty accessing health care or would prefer the convenience of less frequent injections. **Conclusion:** PP6M with its long duration of action and lowered frequency of administration (once every 6 months) expands the therapeutic choices available to patients with schizophrenia. More studies in patients with schizophrenia with PP6M, and perhaps other mental illnesses (eg, schizoaffective disorder), are required to fully elucidate the therapeutic potential of PP6M.

Cirnigliaro G, Battini V, Castiglioni M, Renne M, Mosini G, Cheli S, Carnovale C,

Dell'Osso B. Evaluating the 6-month formulation of paliperidone palmitate: a twice-yearly injectable treatment for schizophrenia in adults. Expert Rev Neurother. 2024 Apr;24(4):325-332. DOI: 10.1080/14737175.2024.2325655. Epub 2024 Mar 6. PMID: 38445396.

Introduction: Paliperidone Palmitate is the only antipsychotic that has been developed in three different intramuscular long-acting injectable (LAI) dosing regimen: monthly (PP1M), quarterly (PP3M), and from 2020 also twice-yearly (PP6M). The latter was approved for the maintenance treatment of adults with schizophrenia and clinically stabilized with PP1M or PP3M.

Areas covered: Data from studies evaluating efficacy in the maintenance treatment of schizophrenia with PP6M are reviewed. Since no post-marketing safety studies are currently available, data from spontaneous reporting system databases, FAERS and Eudravigilance, are analyzed and the reported treatment-emergent adverse events of PP6M are discussed.

Expert opinion: The efficacy of PP6M is comparable to that of PP3M in terms of relapses prevention in patients with schizophrenia previously stabilized on PP3M or PP1M. Also, the maintenance of clinical efficacy in the long term has been demonstrated. Data from pharmacovigilance analyses, as well as from phase 3 studies, show that PP6M is generally well tolerated, consistently with PP3M safety data. PP6M allows a longer dosing interval than any other LAI antipsychotics, potentially reducing nonadherence and disease relapses. In future, an increase in the prescription rates of PP6M is expected and real-world efficacy and tolerability studies will be conducted.

Additional documents

No documents were uploaded

Useful links

There are no additional links

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

Paliperidone is an atypical antipsychotic drug indicated for the treatment of both schizophrenia & schizoaffective disorder. Paliperidone is the primary active metabolite of risperidone and functions by strongly binding to dopaminergic D2- and serotonergic 5-HT2-receptors and selectively blocking monoamine effects. Although paliperidone is a potent D2-antagonist, it has less of impact on motor function and catalepsy than traditional neuroleptics. Paliperidone palmitate is the palmitate ester prodrug of paliperidone and displays modest solubility in polar solvents. Several long-acting injectable aqueous nanocrystal formulations of paliperidone palmitate are available as once-monthly (PP1M), three-monthly (PP3M) and six-monthly (PP6M) extended-release suspensions for intramuscular injection.