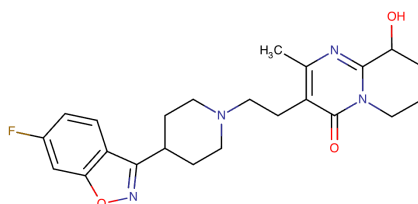


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# Paliperidone Palmitate Three Monthly (PP3M)

## Developer(s)

Janssen/Johnson & Johnson

Originator

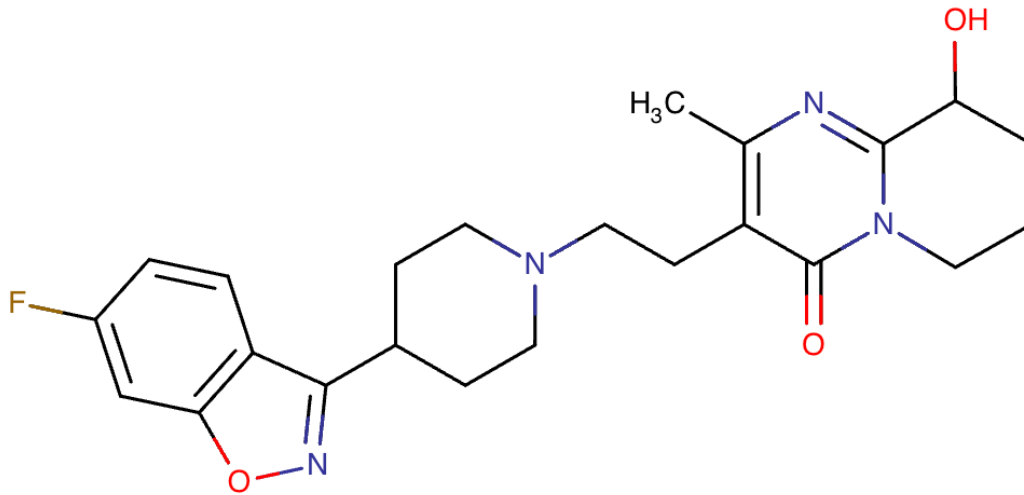
<https://www.janssen.com/>

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.

## Drug structure



Paliperidone Chemical Structure

Sourced From DrugBank

# Drug information

## Associated long-acting platforms

Nanocrystal technology, Aqueous drug particle suspension

## 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

### Frequency of administration

Not provided

### User acceptance

Not provided

### Dosage

## **Available dose and strength**

Not provided

## **Maximum dose**

Not provided

## **Recommended dosing regimen**

Not provided

## **Additional comments**

Not provided

## **Dosage link(s)**

Not provided

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## **Drug information**

### **Drug's link(s)**

Not provided

### **Generic name**

Paliperidone Palmitate Three-Monthly (PP3M)

### **Brand name**

INVEGA TRINZA®, TREVICTA® (previously Paliperidone Janssen)

### **Compound type**

Small molecule

### **Drug class/category**

Not provided

### **Summary**

Paliperidone palmitate administered as a once every three-month long-acting injectable (PP3M) is indicated for the maintenance treatment of schizophrenia in patients who have achieved a satisfactory therapeutic response following at least four months of continuous treatment with one-monthly paliperidone palmitate (PP1M) injection. INVEGA TRINZA® and TREVICTA® manufactured by Janssen Pharmaceuticals are available in dosage formulations of 273 mg, 410 mg, 546 mg and 819 mg. Due to its extremely low water solubility, PP3M dissolves gradually following intramuscular

injection, prior to being hydrolysed to paliperidone and subsequent absorption. Release of the active paliperidone substance lasts up to 18 months, with maximum plasma concentrations achieved after approx. 30-33 days (median Tmax).

## **Approval status**

PP3M is approved under the trade name of INVEGA TRINZA® 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. PP3M is also approved by the European Medicines Agency (EMA) under the trade name of TREVICTA® (previously Paliperidone Janssen) for the maintenance treatment of schizophrenia in adult patients who are clinically stable on PP1M. Generic formulations of PP3M have not yet been approved in the European Union. PP3M is not currently approved for use in children and adolescents.

## **Regulatory authorities**

Countries where PP3M formulations (INVEGA TRINZA® / TREVICTA®) are approved:

Asia Pacific: Australia, Brunei Darussalam, China, Hong Kong, Indonesia, Japan, Macao, Malaysia, New Zealand, Philippines, Singapore, South Korea, Taiwan, Thailand. EMEA: Albania, Bahrain, Bosnia and Herzegovina, Egypt, European Union, Ghana, Israel, Jordan, Kazakhstan, Kenya, Kuwait, Latvia, Lebanon, Montenegro, Morocco, Norway, Oman, Qatar, Russian Federation, Rwanda, Saudi Arabia, Serbia, South Africa, Sudan, Switzerland, Turkey, United Arab Emirates, United Kingdom. Latin America: Argentina, Aruba, Brazil, Chile, Colombia, Costa Rica, Curaçao, Dominican Republic, Ecuador, El Salvador, Guatemala, Honduras, Jamaica, Mexico, Nicaragua, Panama, Peru, Trinidad and Tobago. North America: Canada, USA.

## **Delivery device(s)**

No delivery device

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# Scale-up and manufacturing prospects

## Scale-up prospects

PP3M is commercially manufactured by Janssen Pharmaceuticals with formulation development provided by Alkermes. The PP3M injectable contains a racemic mixture of (+)- and (-)- of paliperidone, which is joined with palmitic acid through an ester linkage. PP3M, like paliperidone palmitate once-monthly injectable (PP1M), is manufactured using Nanocrystal Technology to improve the dissolution properties of paliperidone palmitate, which is highly insoluble in water. PP3M has an extended dosing interval arising from a higher concentration (312 mg/mL) 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.

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# Clinical trials

Not provided

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# 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

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# Patent info

## Description

Paliperidone palmitate LAI dosing regimen for missed doses in PP1M and switch to 3-months formulation (PP3M: 175 or 525 mg eq., 273 or 819 mg PP)

## Brief description

The present application provides a method for treating patients in need of psychiatric treatment, wherein said patient is being treated with the 3-month formulation of paliperidone palmitate and fails to take the next scheduled dose of the 3-month formulation of paliperidone palmitate.

## Representative patent

WO2016164218

## Category

Dosing regimen

## Patent holder

Janssen

## Exclusivity

Not provided

## Expiration date

March 30, 2026

## **Status**

Granted: AU, CA, EA (AM, AZ, BY, KG, KZ, RU, TJ, TM), EP (AT, BE, BG, CH, CZ, DE, EE, ES, FI, FR, GB, GR, HR, HU, IE, IT, LT, LU, LV, MC, MK, MT, NO, NL, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME, MA, MD), IL, JP, KR, MA, UA, US Pending: KR Not in force: BR, NZ

## **Description**

Paliperidone aqueous suspensions

## **Brief description**

The present invention is concerned with a pharmaceutical composition suitable as a depot formulation for administration via intramuscular or subcutaneous injection, comprising: (1) as an active ingredient a therapeutically effective amount of a 9-hydroxyrisperidone fatty acid ester or a salt, or a stereoisomer or a stereoisomeric mixture thereof and (2) a pharmaceutically acceptable carrier; wherein the pharmaceutically acceptable carrier is water and the active ingredient is suspended therein; and with a process of preparing such a composition. The invention further concerns such a pharmaceutical composition for use as a medicament in the treatment of schizophrenia, non-schizophrenic psychoses, behavioural disturbances associated with neurodegenerative disorders

## **Representative patent**

WO9744039

## **Category**

Composition

## **Patent holder**

Janssen Pharmaceutica, N. V

## **Exclusivity**

Not provided

## **Expiration date**

May 12, 2017

## **Status**

Expired

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# Supporting material

## Publications

Daghistani N, Rey JA. Invega Trinza: The First Four-Times-a-Year, Long-Acting Injectable Antipsychotic Agent. *P T*. 2016 Apr;41(4):222-7. PMID: 27069340; PMCID: PMC4811251.

Paliperidone palmitate three-month injection (Invega Trinza): the first four-times-a-year, long-acting injectable antipsychotic agent for schizophrenia.

Lopez A, Rey J. Role of paliperidone palmitate 3-monthly in the management of schizophrenia: insights from clinical practice. *Neuropsychiatr Dis Treat*. 2019 Feb 11;15:449-456. DOI: 10.2147/NDT.S140383. PMID: 30804673; PMCID: PMC6375110.

Schizophrenia is a complex, chronic psychiatric disorder associated with reduced quality of life and shortened life span. The majority of patients with schizophrenia will relapse within 1 year following an acute episode. The ultimate goals of treatment are to improve functional capabilities, minimize residual symptoms during periods of remission, and decrease relapse frequency and duration, as each relapse brings with it the possibility of a worsening prognosis. Maintaining therapeutic continuity is essential for long-term, positive patient outcomes in schizophrenia. Medication nonadherence and symptomatic relapses magnify the disease burden associated with this disorder. Medication adherence in chronic disease states generally improves with a decrease in dosing frequency. Long-acting injectable (LAI) antipsychotics were developed to improve patient outcomes secondarily to improving medication adherence. Paliperidone palmitate 3-monthly injection (PP3M) is the only LAI available with a quarterly dosing interval. PP3M has been US Food and Drug Administration-approved for use in the long-term maintenance treatment of schizophrenia in patients already controlled on once-monthly PP LAI (paliperidone palmitate once-monthly injection [PP1M]) for a minimum of 4 months. As current evidence supports the efficacy and

tolerability of PP3M compared to PP1M and placebo, PP3M appears to be a viable treatment option for patients previously maintained on PP1M. However, to truly establish the place of PP3M in therapy relative to other oral antipsychotics and LAIs, more research is needed. This narrative review aims briefly to describe the pharmacotherapeutic characteristics of PP3M and summarize current literature pertaining to the use of PP3M in the management of schizophrenia.

## **Additional documents**

No documents were uploaded

## **Useful links**

- [U.S. FDA Approves INVEGA TRINZA™, First and Only Four-Times-A-Year Treatment for Schizophrenia](#)
  - [INVEGA TRINZA - Nano-Particle Technology](#)
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# 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

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## 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-HT<sub>2</sub>-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.