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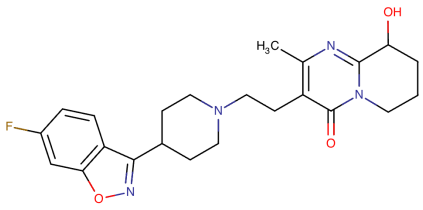


Paliperidone Palmitate Once-Monthly (PP1M)

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.

Neuraxpharm

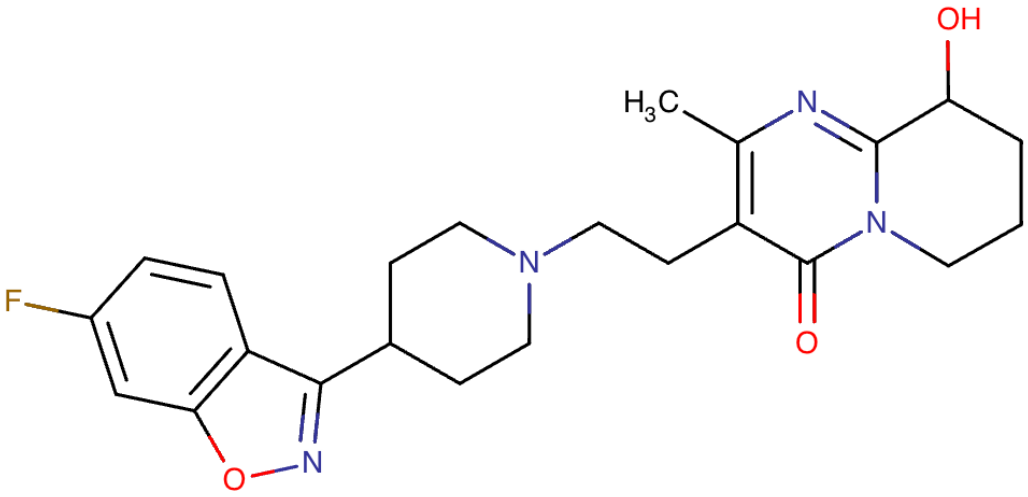
Generic

https://www.neuraxpharm.com/

Spain & Germany

Neruaxpharm is a European biopharmaceutical company headquartered in both Barcelona, Spain and Langenfeld, Germany. Neuraxpharm specialises in developing medicines and generics for diseases of the central nervous system (CNS). Their portfolio consists of more than 120 molecules for the treatment of Anxiety, Depression, Schizophrenia, Epilepsy, Alzheimer’s, Parkinson’s and other CNS disorders.

Drug structure



Paliperidone Chemical 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

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

Drug information

Drug's link(s)

Not provided

Generic name

Paliperidone Palmitate Once-Monthly (PP1M)

Brand name

INVEGA SUSTENNA®, XEPLION®, Niapelf

Compound type

Small molecule

Drug class/category

Not provided

Summary

Paliperidone palmitate administered as a once monthly long-acting injectable (PP1M) is indicated for the maintenance treatment of schizophrenia and schizoaffective disorder. INVEGA SUSTENNA® and XEPLION® are manufactured by Janssen Pharmaceuticals and available in dosage strengths of 25mg, 50mg, 100mg, and 150mg. Prior to the initiation of treatment, oral-lead periods to establish tolerability are required for patients naïve to either oral paliperidone or oral or injectable risperidone. Due to its extremely low water solubility, PP1M dissolves slowly following intramuscular injection,

prior to being hydrolysed to paliperidone and subsequent absorption. Release of the active paliperidone substance lasts up to 4 months, with maximum plasma concentrations achieved after 13 days (median Tmax).

Approval status

PP1M has been approved under the trade name of INVEGA SUSTENNA® (Janssen-Cilag Ltd) by the US Food and Drug Administration for the treatment of schizophrenia (approved Aug 2009) & schizoaffective disorder (approved Nov 2015) as monotherapy and as an adjunct to mood stabilisers or antidepressants. The safety and effectiveness of INVEGA SUSTENNA® in patients < 18 years of age have not been established. PP1M is approved by the European Medicines Agency (EMA) under the trade name XEPLION® (Janssen-Cilag Ltd) for the maintenance treatment of schizophrenia in adults whose disease has already been stabilised on treatment with paliperidone or risperidone. The European Commission granted a marketing authorisation valid throughout the European Union for XEPLION® on 4 March 2011.

Regulatory authorities

PP1M is authorised in 102 countries/territories worldwide as of December 6th 2022.

Delivery device(s)

No delivery device

Scale-up and manufacturing prospects

Scale-up prospects

PP1M is commercially manufactured.

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

Not provided

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

Formulation patent families

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Paliperidone dosing regimen Expiry date: 2028-12-17 The present invention provides a method of treating patients in need of treatment with long acting injectable paliperidone palmitate formulations.	WO2009080651	Dose/Regimen	Janssen Pharmaceutica Nv	No	

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted	Belarus, Azerbaijan, Moldova, Republic of, Armenia, Kazakhstan, Albania, Serbia, Bosnia and Herzegovina, Türkiye, North Macedonia, Ukraine, Malaysia, Philippines, Mexico, Sri Lanka, South Africa	Australia, Canada, Russian Federation, Liechtenstein, Italy, Norway, Malta, Denmark, Belgium, United Kingdom, Greece, Netherlands, Hungary, Croatia, Switzerland, Spain, Slovenia, Austria, Romania, Iceland, Cyprus, Finland, France, Bulgaria, Slovakia, Poland, Latvia, Ireland, Estonia, Germany, Luxembourg, Portugal, Czechia, Lithuania, Monaco, Sweden, Hong Kong, Japan, Korea, Republic of, New Zealand, United States of America, Singapore
Filed	Ecuador, Guatemala, Nicaragua, Indonesia	Finland, Hong Kong, Israel, Korea, Republic of

Patent status/countries	Low, Low- middle and upper-middle	High income
Not in force	World Intellectual Property Organization (WIPO), Brazil, China, Colombia, Tajikistan, Turkmenistan, Kyrgyzstan, Albania, Serbia, Bosnia and Herzegovina, Türkiye, North Macedonia, India	World Intellectual Property Organization (WIPO), Liechtenstein, Italy, Norway, Malta, Denmark, Belgium, United Kingdom, Greece, Netherlands, Hungary, Croatia, Switzerland, Spain, Slovenia, Austria, Romania, Iceland, Cyprus, Finland, France, Bulgaria, Slovakia, Poland, Latvia, Ireland, Estonia, Germany, Luxembourg, Portugal, Czechia, Lithuania, Monaco, Sweden, Israel, United States of America

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Paliperidone depot formulation for injection Expiry date: 2018-11-10 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-hydroxy-risperidone fatty acid ester or a salt, or a stereoisomer or a stereoisomeric mixture thereof in submicron form and (2) a pharmaceuticall 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 psychosis, schizophrenia, schizoaffective disorders, non-schizophrenic psychoses, behavioural disturbances associated with neurodegenerative disorders, e.g. in dementia, behavioural disturbances in mental retardation and autism, Tourette's syndrome, bipolar mania, depression, anxiety.	WO9925354	Composition	Janssen Pharmaceutica N.V	No	

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted		
Filed		

Patent status/countries	Low, Low- middle and upper-middle	High income
Not in force	World Intellectual Property Organization (WIPO), Eswatini, Uganda, Zambia, Zimbabwe, Malawi, Ghana, Sudan, Botswana, Lesotho, Kenya, Gambia (the), Argentina, Brazil, China, Tajikistan, Belarus, Azerbaijan, Moldova, Republic of, Turkmenistan, Armenia, Kyrgyzstan, Kazakhstan, Albania, North Macedonia, Indonesia, Malaysia, Congo, Mauritania, Guinea-Bissau, Niger, Senegal, Cameroon, Mali, Togo, Burkina Faso, Benin, Côte d'Ivoire, Central African Republic, Guinea, Gabon, Chad, Türkiye, Ukraine, South Africa, Viet Nam, Mexico	World Intellectual Property Organization (WIPO), Australia, Bulgaria, Canada, Czechia, Russian Federation, Estonia, Liechtenstein, Italy, Denmark, Belgium, United Kingdom, Greece, Netherlands, Switzerland, Spain, Slovenia, Austria, Romania, Cyprus, Finland, France, Latvia, Ireland, Germany, Luxembourg, Portugal, Lithuania, Monaco, Sweden, Hong Kong, Croatia, Hungary, Israel, Japan, Korea, Republic of, Norway, New Zealand, Poland, Slovakia, United States of America, Singapore, Brunei Darussalam

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Paliperidone aqueous suspensions Expiry date: 2017-05-12 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, e.g. in dementia, behavioural disturbances in mental retardation and autism, bipolar mania, depression, anxiety.	WO9744039	Composition	JANSSEN PHARMACEUTICA NV [BE]	No	

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted		
Filed		

Patent status/countries	Low, Low- middle and upper-middle	High income
Not in force	World Intellectual Property Organization (WIPO), Argentina, Brazil, China, Tajikistan, Belarus, Azerbaijan, Moldova, Republic of, Turkmenistan, Armenia, Kyrgyzstan, Kazakhstan, Albania, Indonesia, Mexico, Malaysia, Türkiye, Ukraine, South Africa	World Intellectual Property Organization (WIPO), Australia, Bulgaria, Canada, Cyprus, Czechia, Germany, Russian Federation, Estonia, Liechtenstein, Italy, Denmark, Belgium, United Kingdom, Greece, Netherlands, Switzerland, Spain, Slovenia, Austria, Romania, Finland, France, Latvia, Ireland, Luxembourg, Portugal, Lithuania, Monaco, Sweden, Hong Kong, Croatia, Hungary, Israel, Japan, Korea, Republic of, Norway, New Zealand, Poland, Slovakia, Taiwan, Province of China, United States of America

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Paliperidone compound and analogues and their use as antipsychotics Expiry date: 2009-10-16 There is disclosed a process for preparing an enantiomeric form of the compound having the formula:or a pharmaceutically acceptable acid addition salt thereof,wherein said process comprises the steps of:(a) reacting a racemic mixture of said compound with a chiral acid or acid chloride selected from the group consisting of tartaric acid, malic acid, mandelic acid, camphor sulfonic acid, 4,5-dihydro-1H-2-benzopyran-2-carboxylic acid, and the acid chlorides thereof, to form a mixture of diastereomeric salts or esters;(b) physically separating said mixture of diastereomeric salts or esters by selective crystallization or chromatography; and(c) converting said separated diastereomeric salts or esters into the corresponding enantiomeric forms of said compound by hydrolysis in an acidic or basic aqueous medium.	CA2000786	Compound	Janssen Pharmaceutica, N. V	No	

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted		
Filed		

Patent status/countries	Low, Low- middle and upper-middle	High income
Not in force	South Africa	Canada, Australia, Chile, Cyprus, Germany, Denmark, Liechtenstein, Italy, Belgium, United Kingdom, Greece, Netherlands, Switzerland, Spain, Austria, France, Luxembourg, Sweden, Finland, Hong Kong, Ireland, Israel, Japan, Korea, Republic of, Norway, New Zealand, Portugal, United States of America

Supporting material

Publications

Bishara D. Once-monthly paliperidone injection for the treatment of schizophrenia. Neuropsychiatr Dis Treat. 2010 Sep 7;6:561-72. doi: 10.2147/NDT.S8505. PMID: 20856919; PMCID: PMC2938305.

Paliperidone palmitate is a new long-acting antipsychotic injection for the treatment of acute and maintenance therapy in schizophrenia. Paliperidone (9-hydroxyrisperidone) is the major active metabolite of risperidone and acts at dopamine D2 and serotonin 5HT2A receptors. As with other atypical antipsychotics, it exhibits a high 5HT2A:D2 affinity ratio. It also has binding activity as an antagonist at α1-and α2 adrenergic receptors and H1 histaminergic receptors, but has virtually no affinity for cholinergic receptors. Paliperidone palmitate has been shown to be effective in reducing Positive and Negative Syndrome Scale total scores in four short-term trials in acute schizophrenia. It was also effective as maintenance therapy in a long-term trial in which time to recurrence of symptoms was significantly longer in paliperidone-treated patients compared with placebo. In addition, paliperidone was shown to be noninferior to risperidone long-acting injection in one study, but this noninferiority was not established in another longer study comparing the two drugs. Treatment should be initiated with 234 mg on day 1 and 156 mg on day 8, followed by a recommended monthly maintenance dose of 39–234 mg based on efficacy and tolerability. Paliperidone palmitate is generally well tolerated, although it can cause weight gain and a rise in prolactin levels, which is generally greater in women than in men. Overall, paliperidone palmitate may have advantages over other currently available long-acting injections, and therefore may be a useful alternative for the treatment of schizophrenia, although further long-term trials comparing it with active treatments are warranted.

Additional documents

No documents were uploaded

Useful links

- https://www.invegasustennahcp.com/
- Niapelf : EPAR - Public assessment report

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

Three bioequivalence studies were conducted to compare Niapelf (a generic paliperidone palmitate prolonged-release injectable suspension) to the reference PP1M product. Two pivotal studies (TOL3033D and TOL3033B) demonstrated bioequivalence through 90% CIs for geometric LS mean ratio of test vs. reference within the acceptance range of 80.00%-125.00% for PK parameters (e.g. AUC0-∞, AUC0-τ, Cmax,ss and Cτ,ss). The TOL3033A study was considered supportive due to a lack of statistical power after excluding a significant number of subjects following methodological deficiencies and GCP non-compliance. Notably, the test product (Niapelf) exhibits consistently lower exposure across all three BE studies (TOL3033D, TOL3033B, TOL3033A), however it was considered unlikely to be of clinical relevance.