

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use INVEGA® SUSTENNA® safely and effectively. See full prescribing information for INVEGA® SUSTENNA®.

INVEGA® SUSTENNA® (paliperidone palmitate) extended-release injectable suspension, for intramuscular use
Initial U.S. Approval: 2006

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

See full prescribing information for complete boxed warning.

- Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. (5.1)
- INVEGA® SUSTENNA® is not approved for use in patients with dementia-related psychosis. (5.1)

RECENT MAJOR CHANGES

Indications and Usage (1) 11/2014
Dosage and Administration (2.2, 2.3) 11/2014

INDICATIONS AND USAGE

INVEGA® SUSTENNA® is an atypical antipsychotic indicated for

- Treatment of schizophrenia. (1)
- Treatment of schizoaffective disorder as monotherapy and as an adjunct to mood stabilizers or antidepressants. (1)

DOSAGE AND ADMINISTRATION

- For intramuscular injection only. (2.1)
- Each injection must be administered only by a health care professional. (2.1)
- For deltoid injection, use 1-inch 23G needle for patients weighing less than 90 kg or 1½-inch 22G needle for patients weighing 90 kg or more. For gluteal injection, use 1½-inch 22G needle regardless of patient weight. (2.1)

Indication	Initiation Dosing (deltoid)		Monthly Maintenance Dose ^a (deltoid or gluteal)	Maximum Monthly Dose
	Day 1	Day 8		
Schizophrenia (2.2)	234 mg	156 mg	39-234 mg ^b	234 mg
Schizoaffective disorder (2.2)	234 mg	156 mg	78-234 mg ^c	234 mg

^a Administered 5 weeks after the first injection.

^b The recommended maintenance dose for treatment of schizophrenia is 117 mg. Some patients may benefit from lower or higher maintenance doses within the additional available strengths (39 mg, 78 mg, 156 mg, and 234 mg).

^c Adjust dose based on tolerability and/or efficacy using available strengths. The 39 mg strength was not studied in the long-term schizoaffective disorder study.

- For patients naïve to oral paliperidone or oral or injectable risperidone, establish tolerability with oral paliperidone or oral risperidone prior to initiating treatment with INVEGA® SUSTENNA®. (2.2)
- Missed Doses: To manage either a missed second initiation dose or a missed monthly maintenance dose, refer to the Full Prescribing Information. (2.3)
- Moderate to severe renal impairment (creatinine clearance < 50 mL/min): INVEGA® SUSTENNA® is not recommended. (2.5)
- Mild renal impairment (creatinine clearance ≥ 50 mL/min to < 80 mL/min): Administer 156 mg on treatment day 1 and 117 mg one week later, both administered in the deltoid muscle. Follow with monthly injections of 78 mg in either the deltoid or gluteal muscle. (2.5)

DOSAGE FORMS AND STRENGTHS

Extended-release injectable suspension: 39 mg, 78 mg, 117 mg, 156 mg, or 234 mg (3)

CONTRAINDICATIONS

Known hypersensitivity to paliperidone, risperidone, or to any excipients in the formulation (4)

WARNINGS AND PRECAUTIONS

- **Cerebrovascular Adverse Reactions, Including Stroke, in Elderly Patients with Dementia-Related Psychosis:** Increased incidence of cerebrovascular adverse reactions (e.g. stroke, transient ischemic attack, including fatalities). INVEGA® SUSTENNA® is not approved for use in patients with dementia-related psychosis (5.2)
- **Neuroleptic Malignant Syndrome:** Manage with immediate discontinuation of drug and close monitoring (5.3)
- **QT Prolongation:** Avoid use with drugs that also increase QT interval and in patients with risk factors for prolonged QT interval (5.4)
- **Tardive Dyskinesia:** Discontinue drug if clinically appropriate (5.5)
- **Metabolic Changes:** Atypical antipsychotic drugs have been associated with metabolic changes that may increase cardiovascular/cerebrovascular risk. These metabolic changes include:
 - **Hyperglycemia and Diabetes Mellitus:** Monitor for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Monitor glucose regularly in patients with diabetes or at risk for diabetes. (5.6)
 - **Dyslipidemia:** Undesirable alterations have been observed. (5.6)
 - **Weight Gain:** Significant weight gain has been reported. Monitor weight gain. (5.6)
- **Orthostatic Hypotension and Syncope:** Use with caution in patients with known cardiovascular or cerebrovascular disease and patients predisposed to hypotension (5.7)
- **Leukopenia, Neutropenia, and Agranulocytosis:** Monitor complete blood count in patients with a history of a clinically significant low white blood cell count (WBC) or a drug-induced leukopenia/neutropenia. Consider discontinuation if clinically significant decline in WBC in the absence of other causative factors (5.8)
- **Hyperprolactinemia:** Prolactin elevations occur and persist during chronic administration (5.9)
- **Potential for Cognitive and Motor Impairment:** Use caution when operating machinery (5.10)
- **Seizures:** Use cautiously in patients with a history of seizures or with conditions that lower the seizure threshold (5.11)

ADVERSE REACTIONS

The most common adverse reactions (incidence ≥ 5% and occurring at least twice as often as placebo) were injection site reactions, somnolence/sedation, dizziness, akathisia, and extrapyramidal disorder. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Janssen Pharmaceuticals, Inc. at 1-800-JANSSEN (1-800-526-7736) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

DRUG INTERACTIONS

- Drugs that may cause orthostatic hypotension: An additive effect may occur when co-administered with INVEGA® SUSTENNA®. (7.1)
- Strong CYP3A4/P-glycoprotein (P-gp) inducers: It may be necessary to increase the dose of INVEGA® SUSTENNA® when a strong inducer of both CYP3A4 and P-gp (e.g., carbamazepine, rifampin, St John's wort) is co-administered. Conversely, on discontinuation of the strong inducer, it may be necessary to decrease the dose of INVEGA® SUSTENNA®. (7.2, 12.3)

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** Based on animal data, may cause fetal harm. (8.1)
 - **Nursing Mothers:** Discontinue drug or nursing, taking into consideration the importance of drug to the mother. (8.3)
- See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: MM/20YY

FULL PRESCRIBING INFORMATION: CONTENTS*

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

1 INDICATIONS AND USAGE

2 DOSAGE AND ADMINISTRATION

- 2.1 Administration Instructions
- 2.2 Schizophrenia and Schizoaffective Disorder
- 2.3 Missed Doses
- 2.4 Use with Risperidone or with Oral Paliperidone
- 2.5 Dosage Adjustments
- 2.6 Switching from Other Antipsychotics
- 2.7 Instructions for Use

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

- 5.1 Increased Mortality in Elderly Patients with Dementia-Related Psychosis
- 5.2 Cerebrovascular Adverse Reactions, Including Stroke, in Elderly Patients with Dementia-Related Psychosis
- 5.3 Neuroleptic Malignant Syndrome
- 5.4 QT Prolongation
- 5.5 Tardive Dyskinesia
- 5.6 Metabolic Changes
- 5.7 Orthostatic Hypotension and Syncope
- 5.8 Leukopenia, Neutropenia, and Agranulocytosis
- 5.9 Hyperprolactinemia
- 5.10 Potential for Cognitive and Motor Impairment
- 5.11 Seizures
- 5.12 Dysphagia
- 5.13 Priapism
- 5.14 Disruption of Body Temperature Regulation

6 ADVERSE REACTIONS

- 6.1 Clinical Trials Experience
- 6.2 Postmarketing Experience
- 6.3 Adverse Reactions Reported With Risperidone

7 DRUG INTERACTIONS

- 7.1 Potential for INVEGA® SUSTENNA® to Affect Other Drugs

- 7.2 Potential for Other Drugs to Affect INVEGA® SUSTENNA®

8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy
- 8.2 Labor and Delivery
- 8.3 Nursing Mothers
- 8.4 Pediatric Use
- 8.5 Geriatric Use
- 8.6 Renal Impairment
- 8.7 Hepatic Impairment
- 8.8 Patients with Parkinson's Disease or Lewy Body Dementia

9 DRUG ABUSE AND DEPENDENCE

- 9.1 Controlled Substance
- 9.2 Abuse
- 9.3 Dependence

10 OVERDOSAGE

- 10.1 Human Experience
- 10.2 Management of Overdosage

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

14 CLINICAL STUDIES

- 14.1 Schizophrenia
- 14.2 Schizoaffective Disorder

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

ENDNOTE ANNOTATIONS

*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

- Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death [see *Warnings and Precautions* (5.1)].
- INVEGA[®] SUSTENNA[®] is not approved for use in patients with dementia-related psychosis [see *Warnings and Precautions* (5.1)].

1 INDICATIONS AND USAGE

INVEGA[®] SUSTENNA[®] (paliperidone palmitate) is indicated for the treatment of:

- Schizophrenia [see *Clinical Studies* 14.1].
- Schizoaffective disorder as monotherapy and as an adjunct to mood stabilizers or antidepressants [see *Clinical Studies* 14.2].

2 DOSAGE AND ADMINISTRATION

2.1 Administration Instructions

Each injection must be administered only by a health care professional.

Parenteral drug products should be inspected visually for foreign matter and discoloration prior to administration, whenever product and container permit.

INVEGA[®] SUSTENNA[®] is intended for intramuscular use only. Do not administer by any other route. Avoid inadvertent injection into a blood vessel. Administer the dose in a single injection; do not administer the dose in divided injections. Inject slowly, deep into the muscle.

The recommended needle size for administration of INVEGA[®] SUSTENNA[®] into the deltoid muscle is determined by the patient's weight:

- For patients weighing less than 90 kg, the 1-inch, 23 gauge needle is recommended.
- For patients weighing 90 kg or more, the 1½-inch, 22 gauge needle is recommended.

Deltoid injections should be alternated between the two deltoid muscles.

The recommended needle size for administration of INVEGA[®] SUSTENNA[®] into the gluteal muscle is the 1½-inch, 22 gauge needle regardless of patient weight.

Administer into the upper-outer quadrant of the gluteal muscle. Gluteal injections should be alternated between the two gluteal muscles.

2.2 Schizophrenia and Schizoaffective Disorder

For patients who have never taken oral paliperidone or oral or injectable risperidone, it is recommended to establish tolerability with oral paliperidone or oral risperidone prior to initiating treatment with INVEGA® SUSTENNA®.

The recommended dosing of INVEGA® SUSTENNA® for each approved indication is displayed in Table 1. The recommended initiation of INVEGA® SUSTENNA® is with a dose of 234 mg on treatment day 1 and 156 mg one week later, both administered in the deltoid muscle. Following the second initiation dose, monthly maintenance doses can be administered in either the deltoid or gluteal muscle.

Table 1. Recommended Dosing of INVEGA® SUSTENNA® for Adults with Schizophrenia or Schizoaffective Disorder

Indication	Initiation Dosing (deltoid)		Monthly Maintenance Dose ^a (deltoid or gluteal)	Maximum Monthly Dose
	Day 1	Day 8		
Schizophrenia	234 mg	156 mg	39-234 mg ^b	234 mg
Schizoaffective disorder	234 mg	156 mg	78-234 mg ^c	234 mg

^a Administered 5 weeks after the first injection.

^b The recommended maintenance dose for treatment of schizophrenia is 117 mg. Some patients may benefit from lower or higher maintenance doses within the additional available strengths (39 mg, 78 mg, 156 mg, and 234 mg).

^c Adjust dose based on tolerability and/or efficacy using available strengths. The 39 mg strength was not studied in the long-term schizoaffective disorder study.

Adjustment of the maintenance dose may be made monthly. When making dose adjustments, the prolonged-release characteristics of INVEGA® SUSTENNA® should be considered [see *Clinical Pharmacology (12.3)*], as the full effect of the dose adjustment may not be evident for several months.

2.3 Missed Doses

Avoiding Missed Doses

It is recommended that the second initiation dose of INVEGA® SUSTENNA® be given one week after the first dose. To avoid a missed dose, patients may be given the second dose 4 days before or after the one-week time point. Similarly, the third and subsequent injections after the initiation regimen are recommended to be given monthly. To avoid a missed monthly dose, patients may be given the injection up to 7 days before or after the monthly time point.

Management of a Missed Second Initiation Dose

If the target date for the second INVEGA[®] SUSTENNA[®] injection (one week \pm 4 days) is missed, the recommended reinitiation depends on the length of time which has elapsed since the patient's first injection. In case of a missed second initiation dose follow the dosing instructions provided in Table 2.

Table 2. Management of a Missed Second Initiation Dose

TIMING OF MISSED SECOND INITIATION DOSE	DOSING
Less than 4 weeks since first injection	Administer the second initiation dose of 156 mg in the deltoid muscle as soon as possible. <ol style="list-style-type: none">1. It is recommended to administer a third injection of 117 mg in either the deltoid or gluteal muscle 5 weeks after the first injection (regardless of the timing of the second injection).2. Thereafter, resume regular monthly dosing in either the deltoid or gluteal muscle.
4 to 7 weeks since first injection	Resume dosing with two injections of 156 mg in the following manner: <ol style="list-style-type: none">1. Administer a deltoid injection as soon as possible.2. Administer a second deltoid injection 1 week later.3. Thereafter, resume regular monthly dosing in either the deltoid or gluteal muscle.
More than 7 weeks since first injection	Restart dosing with recommended initiation (see Section 2.2, Table 1): <ol style="list-style-type: none">1. Administer a 234 mg deltoid injection on Day 1.2. Administer a 156 mg deltoid injection 1 week later.3. Thereafter, resume regular monthly dosing in either the deltoid or gluteal muscle.

Management of a Missed Maintenance Dose

In case of a missed maintenance dose follow the dosing instructions provided in Table 3.

Table 3. Management of a Missed Maintenance Dose

TIMING OF MISSED MAINTENANCE DOSE	DOSING
4 to 6 weeks since last injection	Resume regular monthly dosing as soon as possible at the patient's previously stabilized dose, followed by injections at monthly intervals.
More than 6 weeks to 6 months since last injection	Resume the same dose the patient was previously stabilized on (unless the patient was stabilized on a dose of 234 mg, then the first 2 injections should each be 156 mg) in the following manner: <ol style="list-style-type: none">1. Administer a deltoid injection as soon as possible.

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.