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----------

Dosage and Administration, Recommended Dosing (2.2)	08/2012
Dosage and Administration, Missed Doses (2.3)	08/2012
Dosage and Administration, Switching from Other Antipsychotics (2.7)	08/2012

----------INDICATIONS AND USAGE----------

INVEGA® SUSTENNA® is an atypical antipsychotic indicated for the treatment of schizophrenia (1)

----------DOSAGE AND ADMINISTRATION----------

- For intramuscular injection only. (2.1)
- For deltoid injection, use 1 ½-inch 22G needle for patients ≥ 90 kg or 1-inch 23G needle for patients < 90 kg. For gluteal injection, use 1 ½-inch 22G needle regardless of patient weight. (2.1)
- 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)
- Initiate dosing with 234 mg on treatment day 1 and 156 mg one week later, both administered in the deltoid muscle. (2.2)
- Recommended monthly maintenance dose 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). Administer monthly maintenance doses in either the deltoid or gluteal muscle. (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 components 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----------

- Centrally-acting drugs: Use caution when co-administering with INVEGA® SUSTENNA®. Avoid alcohol. (7.1)
- Drugs that may cause orthostatic hypotension: An additive effect may occur when co-administered with INVEGA® SUSTENNA®. (7.1)
- Strong CYP3A4 inducers: It may be necessary to increase the dose of INVEGA® SUSTENNA® when a CYP3A4 strong inducer (e.g., carbamazepine, rifampin, St John's wort) is added. It may be necessary to decrease the dose when a CYP3A4 strong inducer is discontinued. (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: 08/2012

FULL PRESCRIBING INFORMATION: CONTENTS*

*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. Efficacy was established in four short-term studies and one longer-term study in adults *[see Clinical Studies (14)]*.

2 DOSAGE AND ADMINISTRATION

2.1 Administration Instructions

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 intravascularly or subcutaneously. Avoid inadvertent injection into a blood vessel. Each injection must be administered only by a health care professional. 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 those ≥ 90 kg, the 1½-inch, the 22 gauge needle is recommended. For those < 90 kg, the 1-inch, the 23 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. Administer into the upper-outer quadrant of the gluteal muscle. Gluteal injections should be alternated between the two gluteal muscles.

2.2 Recommended Dosing

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®.

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. The recommended

monthly maintenance dose is 117 mg; however, based on previous clinical history of tolerability and/or efficacy, some patients may benefit from lower or higher maintenance doses within the additional available strengths (39 mg, 78 mg, 156 mg, and 234 mg). Following the second dose, monthly maintenance doses can be administered in either the deltoid or gluteal muscle.

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.

If the target date for the second INVEGA® SUSTENNA® injection (one week ± 4 days) is missed, the recommended reinitiation depends on the length of time which has elapsed since the patient's first injection.

Missed second initiation dose (< 4 weeks from first injection)

If less than 4 weeks have elapsed since the first injection, then the patient should be administered the second injection of 156 mg in the deltoid muscle as soon as possible. A third INVEGA® SUSTENNA® injection of 117 mg is recommended in either the deltoid or gluteal muscle administered 5 weeks after the first injection (regardless of the timing of the second injection). The normal monthly cycle of injections in either the deltoid or gluteal muscle of 39 mg to 234 mg based on individual patient tolerability and/or efficacy should be followed thereafter.

Missed second initiation dose (4-7 weeks from first injection)

If 4 to 7 weeks have elapsed since the first injection of INVEGA® SUSTENNA®, resume dosing with two injections of 156 mg in the following manner: a deltoid injection as soon as possible followed by another deltoid injection one week later, then resumption of the normal monthly cycle of injections in either the deltoid or gluteal muscle of 39 mg to 234 mg based on individual patient tolerability and/or efficacy.

Missed second initiation dose (> 7 weeks from first injection)

If more than 7 weeks have elapsed since the first injection of INVEGA® SUSTENNA®, initiate dosing as described in Section 2.1 above.

Missed Maintenance Dose (1 Month to 6 Weeks)

After initiation, the recommended injection cycle of INVEGA® SUSTENNA® is monthly. If less than 6 weeks have elapsed since the last injection, then the previously stabilized dose should be administered as soon as possible, followed by injections at monthly intervals.

Missed Maintenance Dose (> 6 Weeks to 6 Months)

If more than 6 weeks have elapsed since the last injection of INVEGA® SUSTENNA®, **resume the same dose the patient was previously stabilized on (unless the patient was stabilized on a dose of 234 mg, then the first two injections should each be 156 mg)** in the following manner: 1) a deltoid injection as soon as practically possible, followed by 2) another deltoid injection (same dose) one week later, and 3) resumption of either deltoid or gluteal dosing at monthly intervals.

Missed Maintenance Dose (> 6 Months)

If more than 6 months have elapsed since the last injection of INVEGA® SUSTENNA®, initiate dosing as described in Section 2.1 above.

2.4 Use with Oral Paliperidone or with Risperidone

Concomitant use of INVEGA® SUSTENNA® with oral paliperidone or oral or injectable risperidone has not been studied. Since paliperidone is the major active metabolite of risperidone, consideration should be given to the additive paliperidone exposure if any of these medications are coadministered with INVEGA® SUSTENNA®.

2.5 Dosage Adjustments

Renal Impairment

INVEGA® SUSTENNA® has not been systematically studied in patients with renal impairment *[see Clinical Pharmacology (12.3)]*. For patients with mild renal impairment (creatinine clearance ≥ 50 mL/min to < 80 mL/min [Cockcroft-Gault Formula]), initiate INVEGA® SUSTENNA® with a dose of 156 mg on treatment day 1 and 117 mg one week later. Administer both doses in the deltoid muscle. Thereafter, follow with monthly injections of 78 mg in either the deltoid or gluteal muscle *[see Use in Specific Populations (8.6) and Clinical Pharmacology (12.3)]*.

INVEGA® SUSTENNA® is not recommended in patients with moderate or severe renal impairment (creatinine clearance < 50 mL/min) *[see Use in Specific Populations (8.6) and Clinical Pharmacology (12.3)]*.

Coadministration with Strong CYP3A4 Inducers

It may be necessary to increase the dose of INVEGA® SUSTENNA® when a CYP3A4 strong inducer (e.g., carbamazepine, rifampin, St John's wort) is added. It may be necessary to decrease

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