Rx only

Single use only

INSTRUCTIONS FOR USE

PLEASE READ COMPLETE INSTRUCTIONS PRIOR TO USE

For deltoid and gluteal intramuscular injection only

Please see Important Safety Information, including Boxed Warning, for INVEGA® SUSTENNA®.

Please see accompanying full Prescribing Information for INVEGA® SUSTENNA®.
**Kit contents**

Each injection must be administered only by a healthcare professional.

The kit contains a prefilled syringe and 2 safety needles for intramuscular injection.

For DELTOID injection:
For patients weighing less than 200 lb (90 kg), use the 1-inch, 23 gauge needle (needle with blue colored hub). For patients weighing 200 lb (90 kg) or more, use the 1½-inch, 22 gauge needle (needle with gray colored hub).

For GLUTEAL injection:
Use the 1½-inch, 22 gauge needle (needle with gray colored hub).

INVEGA® SUSTENNA® is for single use only.

<table>
<thead>
<tr>
<th>DELTOID INJECTION</th>
<th>GLUTEAL INJECTION</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient weight</strong></td>
<td><strong>Needle size</strong></td>
</tr>
<tr>
<td>less than 200 lb (90 kg)</td>
<td>1 inch, 23 gauge</td>
</tr>
<tr>
<td>200 lb (90 kg) or more</td>
<td>1½ inch, 22 gauge</td>
</tr>
<tr>
<td>All weights</td>
<td>1½ inch, 22 gauge</td>
</tr>
</tbody>
</table>
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.

INSTRUCTIONS FOR USE

a. Shake the syringe vigorously for a minimum of 10 seconds to ensure a homogeneous suspension.

b. Select the appropriate needle.

For DELTOID injection: For patients weighing less than 200 lb (90 kg), use the 1-inch, 23 gauge needle (needle with blue colored hub). For patients weighing 200 lb (90 kg) or more, use the 1½-inch, 22 gauge needle (needle with gray colored hub).

For GLUTEAL injection, use the 1½-inch, 22 gauge needle (needle with gray colored hub).
c. While holding the syringe upright, remove the rubber tip cap with an easy clockwise twisting motion.

d. Peel the safety needle pouch half way open. Grasp the needle sheath using the plastic peel pouch. Attach the safety needle to the luer connection of the syringe with an easy clockwise twisting motion.

e. Pull the needle sheath away from the needle with a straight pull. Do not twist the sheath as the needle may be loosened from the syringe.

f. Bring the syringe with the attached needle in an upright position to de-aerate. De-aerate the syringe by moving the plunger rod carefully forward.
g. Inject the entire contents intramuscularly slowly, deep into the selected deltoid or gluteal muscle of the patient. **Do not administer by any other route.**

h. After the injection is complete, use either thumb or finger of one hand (h1, h2) or a flat surface (h3) to activate the needle protection system. The needle protection system is fully activated when a “click” is heard. Discard the syringe with needle appropriately.
DOSAGE AND ADMINISTRATION

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®.

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

<table>
<thead>
<tr>
<th>Indication</th>
<th>Initiation Dosing (deltoid)</th>
<th>Monthly Maintenance Dosea (deltoid or gluteal)</th>
<th>Maximum Monthly Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schizophrenia</td>
<td>234 mg</td>
<td>39-234 mgb</td>
<td>234 mg</td>
</tr>
<tr>
<td>Schizoaffective disorder</td>
<td>234 mg</td>
<td>78-234 mgc</td>
<td>234 mg</td>
</tr>
</tbody>
</table>

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 in the accompanying full Prescribing Information)], as the full effect of the dose adjustment may not be evident for several months.

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. Utilizing this dosing window to help avoid missed doses should be considered the exception rather than the rule, and does not imply that the monthly dosing interval can be changed to 3-week or 5-week cycles.

Please see accompanying full Prescribing Information for additional information regarding management of a missed second initiation Dose (see Section 2.3; Table 2 in the full Prescribing Information) and management of a missed maintenance dose (see Section 2.3; Table 3 in the full Prescribing Information).
Administration Instructions

Each injection must be administered only by a healthcare 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. Administer into the upper-outer quadrant of the gluteal area. Gluteal injections should be alternated between the 2 gluteal muscles.

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®.

Dosage Adjustments

Renal Impairment

INVEGA® SUSTENNA® has not been systematically studied in patients with renal impairment [see Clinical Pharmacology (12.3) in full Prescribing Information]. For patients with mild renal impairment (creatinine clearance $\geq 50$ 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) in full Prescribing Information].

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) in full Prescribing Information].

Coadministration with 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® [see Drug Interactions (7.2) and Clinical Pharmacology (12.3) in full Prescribing Information].

Switching from Other Antipsychotics

There are no systematically collected data to specifically address switching patients with schizophrenia or schizoaffective disorder from other antipsychotics to INVEGA® SUSTENNA®, or concerning concomitant administration with other antipsychotics.
Switching from Oral Antipsychotics
For patients who have never taken oral paliperidone or oral or injectable risperidone, tolerability should be established with oral paliperidone or oral risperidone prior to initiating treatment with INVEGA® SUSTENNA®.

Previous oral antipsychotics can be discontinued at the time of initiation of 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 [see Dosage and Administration (2.2) in the full Prescribing Information]. Patients previously stabilized on different doses of INVEGA® Extended-Release tablets can attain similar paliperidone steady-state exposure during maintenance treatment with INVEGA® SUSTENNA® monthly doses as depicted in Table below.

Doses of INVEGA® and INVEGA® SUSTENNA® needed to attain similar steady-state paliperidone exposure during maintenance treatment

<table>
<thead>
<tr>
<th>Formulation</th>
<th>INVEGA® Extended-Release Tablet</th>
<th>INVEGA® SUSTENNA® Injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosing Frequency</td>
<td>Once Daily</td>
<td>Once every 4 weeks</td>
</tr>
<tr>
<td>Dose (mg)</td>
<td>12</td>
<td>234</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>117</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>39-78</td>
</tr>
</tbody>
</table>

Switching from Long-Acting Injectable Antipsychotics
For patients who have never taken oral paliperidone or oral or injectable risperidone, tolerability should be established with oral paliperidone or oral risperidone prior to initiating treatment with INVEGA® SUSTENNA®.

When switching patients currently at steady-state on a long-acting injectable antipsychotic, initiate INVEGA® SUSTENNA® therapy in place of the next scheduled injection. INVEGA® SUSTENNA® should then be continued at monthly intervals. The one-week initiation dosing regimen as described in Section 2.2 of the accompanying full Prescribing Information is not required. See Table 1 in accompanying full Prescribing Information for recommended monthly maintenance dosing. Based on previous clinical history of tolerability and/or efficacy, some patients may benefit from lower or higher maintenance doses within the available strengths (39 mg, 78 mg, 117 mg, 156 mg, and 234 mg). The 39 mg strength was not studied in the long-term schizoaffective disorder study. Monthly maintenance doses can be administered in either the deltoid or gluteal muscle [see Dosage and Administration (2.2) in the full Prescribing Information].
If INVEGA® SUSTENNA® is discontinued, its prolonged-release characteristics must be considered. As recommended with other antipsychotic medications, the need for continuing existing extrapyramidal symptoms (EPS) medication should be re-evaluated periodically.

Storage and Handling
Store at room temperature (25°C, 77°F).

IMPORTANT RESOURCES
For additional information, visit www.invegasustenna.com or call the Janssen Medical Information Center at 1-800-526-7736.

INVEGA® SUSTENNA® (paliperidone palmitate) is indicated for the treatment of:
- Schizophrenia.
- Schizoaffective disorder as monotherapy and as an adjunct to mood stabilizers or antidepressants.

IMPORTANT SAFETY INFORMATION FOR INVEGA® SUSTENNA® (paliperidone palmitate)

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.
- INVEGA® SUSTENNA® is not approved for the treatment of patients with dementia-related psychosis.

Contraindications: Paliperidone is contraindicated in patients with a known hypersensitivity to either paliperidone, risperidone, or to any excipients of the formulation.

Cerebrovascular Adverse Reactions: Cerebrovascular adverse reactions (e.g., stroke, transient ischemic attacks), including fatalities, were reported in placebo-controlled trials in elderly patients with dementia-related psychosis taking oral risperidone, aripiprazole, and olanzapine. The incidence of cerebrovascular adverse reactions was significantly higher than with placebo. INVEGA® SUSTENNA® is not approved for the treatment of patients with dementia-related psychosis.

Neuroleptic Malignant Syndrome (NMS): NMS, a potentially fatal symptom complex, has been reported with the use of antipsychotic medications, including paliperidone. Clinical manifestations include muscle rigidity, fever, altered mental status, and evidence of autonomic instability (see full Prescribing Information). Management should include immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, intensive symptomatic treatment and close medical monitoring, and treatment of any concomitant serious medical problems.
**QT Prolongation:** Paliperidone causes a modest increase in the corrected QT (QTc) interval. Avoid the use of drugs that also increase QTc interval and in patients with risk factors for prolonged QTc interval. Paliperidone should also be avoided in patients with congenital long QT syndrome and in patients with a history of cardiac arrhythmias. Certain circumstances may increase the risk of the occurrence of torsades de pointes and/or sudden death in association with the use of drugs that prolong the QTc interval.

**Tardive Dyskinesia (TD):** TD is a syndrome of potentially irreversible, involuntary, dyskinetic movements that may develop in patients treated with antipsychotic medications. The risk of developing TD and the likelihood that dyskinetic movements will become irreversible are believed to increase with duration of treatment and total cumulative dose, but can develop after relatively brief treatment at low doses. Elderly female patients appeared to be at increased risk for TD, although it is impossible to predict which patients will develop the syndrome. Prescribing should be consistent with the need to minimize the risk of TD (see full Prescribing Information). Discontinue drug if clinically appropriate. The syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn.

**Metabolic Changes:** Atypical antipsychotic drugs have been associated with metabolic changes that may increase cardiovascular/cerebrovascular risk. These metabolic changes include hyperglycemia, dyslipidemia, and body weight gain. While all of the drugs in the class have been shown to produce some metabolic changes, each drug has its own specific risk profile.

Hyperglycemia and Diabetes Mellitus: Hyperglycemia and diabetes mellitus, in some cases extreme and associated with ketoacidosis, hyperosmolar coma or death, have been reported in patients treated with all atypical antipsychotics (APS). Patients starting treatment with APS who have or are at risk for diabetes mellitus should undergo fasting blood glucose testing at the beginning of and during treatment. Patients who develop symptoms of hyperglycemia during treatment should also undergo fasting blood glucose testing. All patients treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia. Some patients require continuation of antidiabetic treatment despite discontinuation of the suspect drug.

Dyslipidemia: Undesirable alterations have been observed in patients treated with atypical antipsychotics.

Weight Gain: Weight gain has been observed with atypical antipsychotic use. Clinical monitoring of weight is recommended.

**Orthostatic Hypotension and Syncope:** INVEGA® SUSTENNA® may induce orthostatic hypotension in some patients due to its alpha-blocking activity. INVEGA® SUSTENNA® should be used with caution in patients with known cardiovascular disease, cerebrovascular disease or conditions that would predispose patients to hypotension (e.g., dehydration, hypovolemia, treatment with antihypertensive medications). Monitoring should be considered in patients for whom this may be of concern.

**Leukopenia, Neutropenia and Agranulocytosis** have been reported with antipsychotics, including paliperidone. Patients with a history of clinically significant low white
blood cell count (WBC) or drug-induced leukopenia/neutropenia should have frequent complete blood cell counts during the first few months of therapy. At the first sign of a clinically significant decline in WBC, and in the absence of other causative factors, discontinuation of INVEGA® SUSTENNA® should be considered. Patients with clinically significant neutropenia should be carefully monitored for fever or other symptoms or signs of infection and treated promptly if such symptoms or signs occur. Patients with severe neutropenia (absolute neutrophil count <1000/mm³) should discontinue INVEGA® SUSTENNA® and have their WBC followed until recovery.

**Hyperprolactinemia:** As with other drugs that antagonize dopamine D₂ receptors, INVEGA® SUSTENNA® elevates prolactin levels, and the elevation persists during chronic administration. Paliperidone has a prolactin-elevating effect similar to risperidone, which is associated with higher levels of prolactin elevation than other antipsychotic agents.

**Potential for Cognitive and Motor Impairment:** Somnolence, sedation, and dizziness were reported as adverse reactions in subjects treated with INVEGA® SUSTENNA®. INVEGA® SUSTENNA® has the potential to impair judgment, thinking, or motor skills. Patients should be cautioned about performing activities that require mental alertness such as operating hazardous machinery, including motor vehicles, until they are reasonably certain that INVEGA® SUSTENNA® does not adversely affect them.

**Seizures:** INVEGA® SUSTENNA® should be used cautiously in patients with a history of seizures or with conditions that potentially lower seizure threshold. Conditions that lower seizure threshold may be more prevalent in patients 65 years or older.

**Administration:** For intramuscular injection only by a healthcare professional. Care should be taken to avoid inadvertent injection into a blood vessel.

**Drug Interactions:** 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®.

**Pregnancy/Nursing:** Patients should be advised to notify their physician if they become pregnant/intend to become pregnant or intend to nurse during treatment with INVEGA® SUSTENNA®.

**Commonly Observed Adverse Reactions for INVEGA® SUSTENNA®:** The most common adverse reactions in clinical trials in patients with schizophrenia (≥5% and twice placebo) were injection site reactions, somnolence/sedation, dizziness, akathisia and extrapyramidal disorder. No adverse events occurred at a rate of ≥5% and twice placebo during the long-term double-blind, placebo-controlled study in patients with schizoaffective disorder. The following adverse reactions occurred more frequently (a ≥2% difference vs. placebo) in the long-term study in patients with schizoaffective disorder: weight increased, nasopharyngitis, headache, hyperprolactinemia, and pyrexia.