
# Dosing & Administration

**INDICATION**
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)**

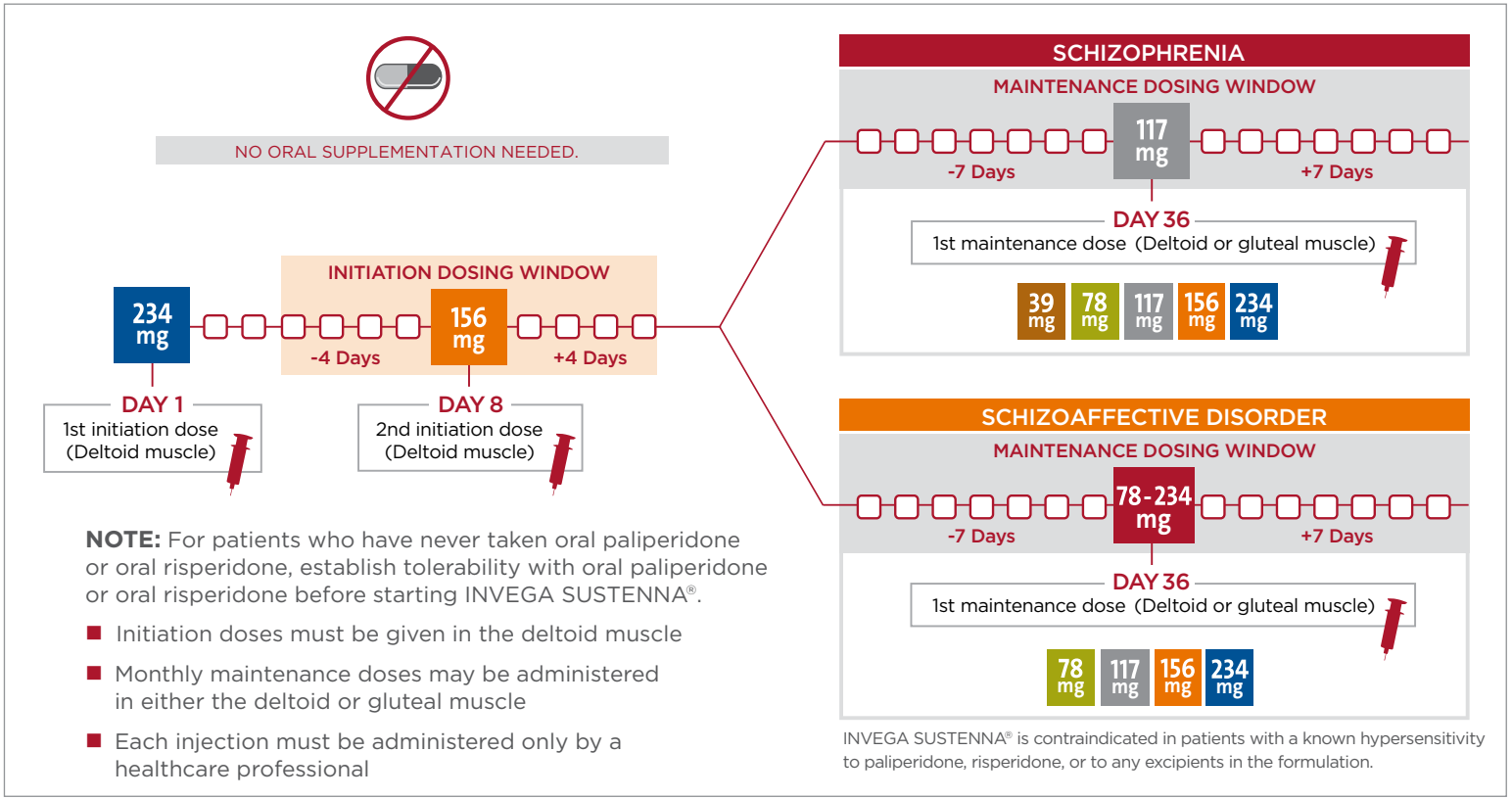
**WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS.**
*See full Prescribing Information for complete Boxed Warning*

- 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.

**Please see Important Safety Information, including Boxed WARNING, starting on page 9.**
**Please see enclosed full Prescribing Information.**

ONCE-MONTHLY
INVEGA SUSTENNA®
paliperidone palmitate extended-release injectable suspension
39mg, 78mg, 117mg, 156mg, 234mg

# Recommended dosing for INVEGA SUSTENNA® (paliperidone palmitate) when initiating or switching from oral antipsychotics




**NOTE:** For patients who have never taken oral paliperidone or oral risperidone, establish tolerability with oral paliperidone or oral risperidone before starting INVEGA SUSTENNA®.

- Initiation doses must be given in the deltoid muscle
- Monthly maintenance doses may be administered in either the deltoid or gluteal muscle
- Each injection must be administered only by a healthcare professional

INVEGA SUSTENNA® is contraindicated in patients with a known hypersensitivity to paliperidone, risperidone, or to any excipients in the formulation.



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## DOSING INFORMATION WHEN SWITCHING FROM ORAL ANTIPSYCHOTICS

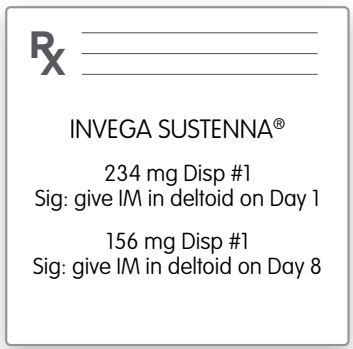
### INITIATION

- Both starting doses must be given in the deltoid muscle
- No oral supplementation is needed
- For patients who have never taken oral paliperidone or oral risperidone, establish tolerability with oral paliperidone or oral risperidone before starting INVEGA SUSTENNA® (paliperidone palmitate)
- Paliperidone is contraindicated in patients with a known hypersensitivity to either paliperidone, risperidone, or to any excipients of the formulation

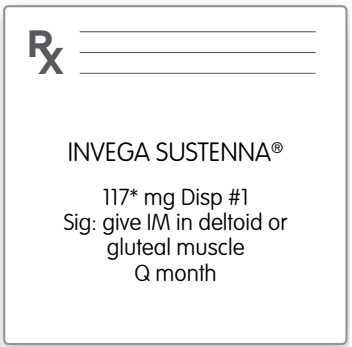
### MAINTENANCE

- Monthly maintenance dose should be administered 5 weeks after the first injection (regardless of the timing of the second injection)
- Utilizing the maintenance dosing window to help avoid missed doses should be considered the exception rather than the rule
- **Schizophrenia:** The recommended maintenance dose for the 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)**
- **Schizoaffective Disorder:** Adjust dose based on tolerability and/or efficacy using available strengths. **The 39 mg strength was not studied in the schizoaffective disorder trial.** For the 164 subjects who were randomized to INVEGA SUSTENNA®, the dose distribution was 78 mg (4.9%), 117 mg (9.8%), 156 mg (47%), and 234 mg (38.4%). **There is no recommended maintenance dose for the treatment of schizoaffective disorder**

WHEN STARTING A PATIENT, INITIATION AND MAINTENANCE SCRIPTS SHOULD BE WRITTEN AT THE SAME TIME AS FOLLOWS:




Initiation




Maintenance

Must be administered only by a healthcare provider.

*117 mg is the recommended maintenance dose for schizophrenia. No recommended maintenance dose for schizoaffective disorder.

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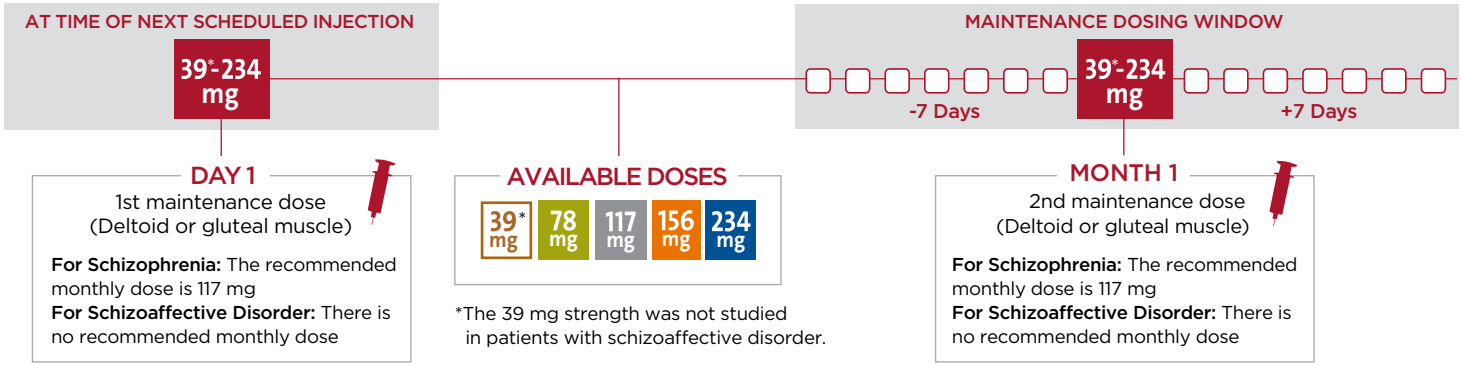
# Recommended dosing for INVEGA SUSTENNA® (paliperidone palmitate) when switching from another long-acting injectable antipsychotic

**INITIATE INVEGA SUSTENNA® THERAPY IN PLACE OF THE NEXT SCHEDULED INJECTION. INVEGA SUSTENNA® SHOULD THEN BE CONTINUED AT MONTHLY INTERVALS.**




**NOTE:** For patients who have never taken oral paliperidone, or oral or injectable risperidone, establish tolerability with oral paliperidone or oral risperidone before starting INVEGA SUSTENNA®.

**When switching patients from another long-acting injectable antipsychotic, the 2 initiation doses are not required.**

INVEGA SUSTENNA® is contraindicated in patients with a known hypersensitivity to paliperidone, risperidone, or to any excipients in the formulation.



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## DOSING INFORMATION WHEN SWITCHING FROM ANOTHER LONG-ACTING INJECTABLE ANTIPSYCHOTIC

- When switching from another long-acting injectable antipsychotic, administer INVEGA SUSTENNA® (paliperidone palmitate) in place of the next injection

### MAINTENANCE DOSING

- **For Schizophrenia:** The recommended monthly 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**
- **For Schizoaffective Disorder:** There is no recommended maintenance dose. **The 39 mg strength was not studied in schizoaffective disorder.** For the 164 subjects who were randomized to INVEGA SUSTENNA®, the dose distribution was 78 mg (4.9%), 117 mg (9.8%), 156 mg (47%), and 234 mg (38.4%)
- Adjustment of the maintenance dose may be made monthly
- Utilizing the maintenance dosing window to help avoid missed doses should be considered the exception rather than the rule

## WHEN SWITCHING, THE FIRST PRESCRIPTION FOR A MAINTENANCE DOSE SHOULD BE WRITTEN AS FOLLOWS:

Rx

INVEGA SUSTENNA®

117* mg Disp #1
Sig: give IM in deltoid or gluteal muscle
Q month

Must be administered only by a healthcare provider.

*117 mg is the recommended maintenance dose for schizophrenia. No recommended maintenance dose for schizoaffective disorder.

**Some patients may benefit from lower or higher maintenance doses within the additional available strengths: 39 mg, 78 mg, 156 mg, and 234 mg.**

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# What to do when the second initiation dose is missed

| TIMING OF MISSED SECOND INITIATION DOSE | ACTION STEPS |
|---|---|
| **<4 weeks** from first injection | **Administer the second initiation dose of 156 mg in the deltoid muscle as soon as possible.**<br>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).<br>2. Resume regular monthly dosing in either the deltoid or gluteal muscle. |
| **4-7 weeks** from first injection | **Resume dosing with 2 injections of 156 mg.**<br>1. Administer a deltoid injection as soon as possible.<br>2. Administer a second deltoid injection 1 week later.<br>3. Resume regular monthly dosing in either the deltoid or gluteal muscle. |
| **>7 weeks** from first injection | **Restart dosing with recommended initiation plan.**<br>1. Administer a 234 mg deltoid injection on Day 1.<br>2. Administer a 156 mg deltoid injection 1 week later.<br>3. Resume regular monthly dosing in either the deltoid or gluteal muscle. |

# What to do when a maintenance dose is missed

| TIMING OF MISSED MAINTENANCE DOSE | ACTION STEPS |
|---|---|
| **4-6 weeks** since last injection | **Resume regular monthly dosing as soon as possible at patient's previously stabilized dose, followed by injections at monthly intervals.** |
| **>6 weeks to 6 months** since last injection | **Continue dosing at patient's previously stabilized dose.***<br>**1.** Administer a deltoid injection as soon as possible.<br>**2.** Administer a second deltoid injection 1 week later at same dose.<br>**3.** Resume administering previously stabilized dose in the deltoid or gluteal muscle 1 month after the second injection.<br>***If patient was stabilized on 234 mg, the first 2 injections should be 156 mg.** |
| **>6 months** since last injection | **Restart dosing with recommended initiation plan.**<br>**1.** Administer a 234 mg deltoid injection on Day 1.<br>**2.** Administer a 156 mg deltoid injection 1 week later.<br>**3.** Resume administering previously stabilized dose in the deltoid or gluteal muscle 1 month after second injection. |



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# What to consider for specific patient populations

## RENAL IMPAIRMENT

- INVEGA SUSTENNA® (paliperidone palmitate) has not been systematically studied in patients with renal impairment
- The dose of INVEGA SUSTENNA® should be reduced in patients with mild renal impairment as it has not been systematically studied in patents with renal impairment
  - For patients with mild renal impairment (creatinine clearance ≥50 mL/min to <80 mL/min), the recommended initiation doses of INVEGA SUSTENNA® are 156 mg on treatment Day 1 and 117 mg 1 week later. Administer both doses in the deltoid muscle
  - Follow with monthly injections of 78 mg in either the deltoid or gluteal muscle
- INVEGA SUSTENNA® is not recommended in patients with moderate or severe renal impairment (creatinine clearance <50 mL/min)

## 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-glycoprotein (eg, carbamazepine, rifampin, St. John's wort) is coadministered. Conversely, on discontinuation of the strong inducer, it may be necessary to decrease the dose of INVEGA SUSTENNA®

## PREGNANCY/NURSING

- Adequate and well-controlled studies with INVEGA SUSTENNA® have not been conducted in pregnant women. Neonates exposed to antipsychotic drugs during the third trimester of pregnancy are at risk for extrapyramidal and/or withdrawal symptoms following delivery
- INVEGA SUSTENNA® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus

## HEPATIC IMPAIRMENT

- INVEGA SUSTENNA® has not been studied in patients with hepatic impairment. Based on a study with oral paliperidone, no dosage adjustment is required in patients with mild or moderate hepatic impairment. Paliperidone has not been studied in patients with severe hepatic impairment


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## ADMINISTRATION INFORMATION

- Each injection must be administered only by a healthcare professional
- INVEGA SUSTENNA® (paliperidone palmitate) is intended for intramuscular use only
- 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
- Paliperidone is contraindicated in patients with a known hypersensitivity to either paliperidone, risperidone, or to any excipients of the formulation

## NOTES

**INVEGA SUSTENNA® is water-soluble.**

**Store at room temperature. No need for refrigeration.**

**Select appropriate needle size depending on patient's weight and injection location.**

**Shake the prefilled syringe for at least 10 seconds before administering.**

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**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.

**Falls:** Somnolence, postural hypotension, motor and sensory instability have been reported with the use of antipsychotics, including INVEGA SUSTENNA®, which may lead to falls and, consequently, fractures or other fall-related injuries. For patients, particularly the elderly, with diseases, conditions, or medications that could exacerbate these effects, assess the risk of falls when initiating antipsychotic treatment and recurrently for patients on long-term antipsychotic therapy.

**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/mm$^3$) should discontinue INVEGA SUSTENNA® and have their WBC followed until recovery.

**Hyperprolactinemia:** As with other drugs that antagonize dopamine $D_2$ 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.

037717-170303

ONCE-MONTHLY

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paliperidone palmitate extended-release injectable suspension

39mg, 78mg, 117mg, 156mg, 234mg

REAL LIFE. REAL RESULTS.

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