Transitioning patients to INVEGA TRINZA®

DOsing AND ADMINISTRATION SUMMARY

IMPORTANT SAFETY INFORMATION and INDICATIONS for INVEGA TRINZA® and INVEGA SUSTENNA®

INVEGA TRINZA® (paliperidone palmitate) a 3-month injection, is an atypical antipsychotic indicated for the treatment of schizophrenia in patients after they have been adequately treated with INVEGA SUSTENNA® (1-month paliperidone palmitate) for at least four months.

INVEGA SUSTENNA® (paliperidone palmitate) is an atypical antipsychotic indicated for the treatment of schizophrenia.

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 TRINZA® and INVEGA SUSTENNA® are not approved for the treatment of patients with dementia-related psychosis

Please see Important Safety Information for INVEGA TRINZA® and INVEGA SUSTENNA® on pages 20 to 22 and full Prescribing Information for INVEGA TRINZA®, including Boxed WARNING, and full Prescribing Information for INVEGA SUSTENNA®, including Boxed WARNING.
Start your patients on a pathway to INVEGA TRINZA®

Oral Antipsychotics

Long-Acting Therapy (LAT) Antipsychotics

INVEGA SUSTENNA® → INVEGA TRINZA®

*Transition to INVEGA TRINZA* (paliperidone palmitate) is seamless after patients have been stabilized on INVEGA SUSTENNA* (paliperidone palmitate) for at least 4 months, based on your evaluation of the patient’s response.¹
With the longest dosing interval offered by INVEGA TRINZA®, you can give your patients greater independence by helping them think less about taking their schizophrenia medication and more about other aspects of their treatment plan.

For patients who you believe would benefit from such a goal, consider starting them on a pathway to INVEGA TRINZA®.

Transition to INVEGA TRINZA® is seamless after patients have been stabilized on INVEGA SUSTENNA® for at least 4 months.†

†Based on your evaluation of the patient’s response.

IMPORTANT SAFETY INFORMATION for INVEGA TRINZA® and INVEGA SUSTENNA®

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

Please see Important Safety Information for INVEGA TRINZA® and INVEGA SUSTENNA® on pages 20 to 22 and full Prescribing Information for INVEGA TRINZA®, including Boxed WARNING, and full Prescribing Information for INVEGA SUSTENNA®, including Boxed WARNING.
TRANSITIONING FROM ORAL ANTIPSYCHOTICS TO INVEGA SUSTENNA® (paliperidone palmitate)²

- If your patients have never taken oral paliperidone or oral or injectable risperidone, it is recommended to establish tolerability prior to initiating treatment with INVEGA SUSTENNA®²
- Previous oral antipsychotics can be gradually discontinued at the time of initiation of treatment with INVEGA SUSTENNA®²
- No need for oral supplementation²
- The recommended initiation of INVEGA SUSTENNA® is with a dose of 234 mg on treatment day 1 and 156 mg 1 week later, both administered in the deltoid muscle²
  - To avoid a missed dose, the second initiation dose may be given within a +/- 4-day flexible window
- Following the second initiation dose, monthly maintenance doses can be administered in either the deltoid or gluteal muscle²
  - To avoid a missed monthly maintenance dose, patients may be given the injection within +/- 7 days of the monthly time point

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**RECOMMENDED DOSING OF INVEGA SUSTENNA® FOR ADULTS WITH SCHIZOPHRENIA TRANSITIONING FROM AN ORAL ANTIPSYCHOTIC²**

<table>
<thead>
<tr>
<th>Initiation dosing (deltoid)</th>
<th>Monthly maintenance dose* (deltoid or gluteal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>Day 8</td>
</tr>
<tr>
<td>234 mg</td>
<td>156 mg</td>
</tr>
</tbody>
</table>

Patients may benefit from lower or higher maintenance doses within the following strengths†: 78 mg, 117 mg, 156 mg, 234 mg.

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*First monthly maintenance dose should be administered 5 weeks after the first injection (regardless of the timing of the second injection).
†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).
‡Conversion from the INVEGA SUSTENNA® 39-mg dose to INVEGA TRINZA® (paliperidone palmitate) was not studied.

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**IMPORTANT²**

- INVEGA SUSTENNA® is intended for intramuscular use only
- Avoid inadvertent injection into a blood vessel
- Administer in a single injection; do not administer in divided injections
- Shake the prefilled syringe for at least 10 seconds before administering
- Inject slowly, deep into the muscle
- Parenteral drug products should be inspected visually for foreign matter and discoloration prior to administration, whenever product and container permit

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Please see Important Safety Information for INVEGA TRINZA® and INVEGA SUSTENNA® on pages 20 to 22 and full Prescribing Information for INVEGA TRINZA®, including Boxed WARNING, and full Prescribing Information for INVEGA SUSTENNA®, including Boxed WARNING.
RECOMMENDED DOSING OF INVEGA SUSTENNA®
FOR ADULTS WITH SCHIZOPHRENIA TRANSITIONING FROM INVEGA®

- 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 using the conversion guide below:

<table>
<thead>
<tr>
<th>Initiation dosing (deltoid)</th>
<th>Monthly maintenance dose* (deltoid or gluteal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>Day 8</td>
</tr>
<tr>
<td>234 mg</td>
<td>156 mg</td>
</tr>
</tbody>
</table>

Patients stabilized on INVEGA® can attain similar steady-state exposure with INVEGA SUSTENNA®

- Please refer to the bottom of page 4 for important information on how to administer INVEGA SUSTENNA®

Dose conversion from INVEGA® to INVEGA SUSTENNA®

<table>
<thead>
<tr>
<th>INVEGA® extended-release tablet (daily)</th>
<th>INVEGA SUSTENNA® injection (once monthly)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 mg</td>
<td>78 mg*</td>
</tr>
<tr>
<td>6 mg</td>
<td>117 mg</td>
</tr>
<tr>
<td>12 mg</td>
<td>234 mg</td>
</tr>
</tbody>
</table>

*First monthly maintenance dose should be administered 5 weeks after the first injection (regardless of the timing of the second injection).

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).

Conversion from the INVEGA SUSTENNA® 39-mg dose to INVEGA TRINZA® was not studied.

IMPORTANT SAFETY INFORMATION and INDICATION for INVEGA®

INVEGA® (paliperidone) extended-release tablets are indicated for the treatment of schizophrenia in adults. The efficacy of INVEGA® in schizophrenia was established in three 6-week trials in adults, as well as one maintenance trial in adults.

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. Analyses of 17 placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (eg, heart failure, sudden death) or infectious (eg, pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear. INVEGA® is not approved for the treatment of patients with dementia-related psychosis.

Please see Important Safety Information for INVEGA® on pages 23 to 25 and full Prescribing Information for INVEGA®, including Boxed WARNING.
TRANSITIONING FROM A LONG-ACTING THERAPY (LAT) ANTIPSYCHOTIC TO INVEGA SUSTENNA® (paliperidone palmitate)

• If your patients have never taken oral paliperidone or oral or injectable risperidone, it is recommended to establish tolerability prior to initiating treatment with INVEGA SUSTENNA®

• Initiate INVEGA SUSTENNA® in place of the next scheduled injection. INVEGA SUSTENNA® should be continued at monthly intervals

• No need for oral supplementation

• Maintenance doses may be administered in either the deltoid or the gluteal muscle
  - To avoid a missed monthly maintenance dose, patients may be given the injection within +/- 7 days of the monthly time point

• Please refer to the bottom of page 4 for important information on how to administer INVEGA SUSTENNA®

<table>
<thead>
<tr>
<th>DOSING OPTIONS FOR INVEGA SUSTENNA® FOR ADULTS WITH SCHIZOPHRENIA TRANSITIONING FROM AN LAT</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Initiation dosing (deltoid)</th>
<th>Monthly maintenance dose* (deltoid or gluteal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>Day 8</td>
</tr>
<tr>
<td>Administer in place of the next scheduled injection: 234 mg†</td>
<td>Not required</td>
</tr>
<tr>
<td>Patients may benefit from lower or higher maintenance doses within the following strengths‡§:</td>
<td></td>
</tr>
<tr>
<td>78 mg</td>
<td>117 mg</td>
</tr>
<tr>
<td>156 mg</td>
<td>234 mg</td>
</tr>
</tbody>
</table>

Some patients may benefit from lower initiation doses:

39 mg 78 mg 117 mg 156 mg

* Administered 1 month after the initial dose.
† The 234-mg INVEGA SUSTENNA® strength was used in the pivotal clinical trial for INVEGA TRINZA® as an initiation dose for patients who were being transitioned from another LAT antipsychotic. Some patients may benefit from lower initiation doses within the available strengths (39 mg, 78 mg, 117 mg, and 156 mg).
‡ 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).
§ Conversion from the INVEGA SUSTENNA® 39-mg dose to INVEGA TRINZA® (paliperidone palmitate) was not studied.

IMPORTANT SAFETY INFORMATION for INVEGA TRINZA® and INVEGA SUSTENNA®

Cerebrovascular Adverse Reactions: Cerebrovascular adverse reactions (e.g., stroke, transient ischemic attacks), including fatalities, were reported at a higher incidence in elderly patients with dementia-related psychosis taking risperidone, aripiprazole, and olanzapine compared to placebo. No studies have been conducted with oral paliperidone, INVEGA SUSTENNA®, or INVEGA TRINZA® in elderly patients with dementia. These medications are not approved for the treatment of patients with dementia-related psychosis.

Please see Important Safety Information for INVEGA TRINZA® and INVEGA SUSTENNA® on pages 20 to 22 and full Prescribing Information for INVEGA TRINZA®, including Boxed WARNING, and full Prescribing Information for INVEGA SUSTENNA®, including Boxed WARNING.
TRANSITIONING FROM RISPERDAL CONSTA® (risperidone) TO INVEGA SUSTENNA®

• Follow recommendations for transitioning patients from LAT antipsychotics

• During the open-label stabilization phase of a long-term maintenance trial for INVEGA TRINZA® for the treatment of schizophrenia, enrolled patients treated with RISPERDAL CONSTA® long-acting injection were switched to INVEGA SUSTENNA® in place of the next scheduled injection at a dose determined by the conversion guide below.

• Please refer to the bottom of page 4 for important information on how to administer INVEGA SUSTENNA®.

<table>
<thead>
<tr>
<th>Initiation dosing (deltoid)</th>
<th>Monthly maintenance dose (deltoid or gluteal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 mg</td>
<td>78 mg</td>
</tr>
<tr>
<td>37.5 mg</td>
<td>117 mg</td>
</tr>
<tr>
<td>50 mg</td>
<td>156 mg</td>
</tr>
<tr>
<td>78 mg</td>
<td>117 mg</td>
</tr>
<tr>
<td>117 mg</td>
<td>156 mg</td>
</tr>
<tr>
<td>156 mg</td>
<td>234 mg</td>
</tr>
</tbody>
</table>

Dose conversion from RISPERDAL CONSTA® to INVEGA SUSTENNA®

<table>
<thead>
<tr>
<th>RISPERDAL CONSTA® injection</th>
<th>INVEGA SUSTENNA® injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 mg</td>
<td>78 mg</td>
</tr>
<tr>
<td>37.5 mg</td>
<td>117 mg</td>
</tr>
<tr>
<td>50 mg</td>
<td>156 mg</td>
</tr>
</tbody>
</table>

Arrows illustrate the corresponding dose conversion from RISPERDAL CONSTA® to INVEGA SUSTENNA®.

1Administered 1 month after the initial dose.

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).

Conversion from the INVEGA SUSTENNA® 39-mg dose to INVEGA TRINZA® was not studied.

Conversion from the RISPERDAL CONSTA® 12.5-mg dose was not studied.

††Dose at study entry.

• It is important to note that the INVEGA SUSTENNA® conversion dose may not reflect the eventual stabilization dose that was achieved during the remainder of the open-label transition phase.

• The prescribing information for INVEGA SUSTENNA® and RISPERDAL CONSTA® do not include conversion charts between these 2 agents.

• Transition dosing was based on internal Janssen pharmacokinetic modeling, and is not included in the INVEGA SUSTENNA® prescribing information.

INDICATION for RISPERDAL CONSTA®

RISPERDAL CONSTA® (risperidone) long-acting injection is indicated for the treatment of schizophrenia.

Please see Important Safety Information for RISPERDAL CONSTA® on pages 26 to 28 and full Prescribing Information for RISPERDAL CONSTA®, including Boxed WARNING.
TRANSITIONING FROM RISPERDAL CONSTA®
(risperidone) TO INVEGA SUSTENNA®
(paliperidone palmitate) (cont’d)

IMPORTANT SAFETY INFORMATION for RISPERDAL CONSTA®

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. Analyses of 17 placebo-controlled trials
(modal duration of 10 weeks), largely in patients taking atypical antipsychotic
drugs, revealed a risk of death in the drug-treated patients of between 1.6 to
1.7 times the risk of death in placebo-treated patients. Over the course of a
typical 10-week controlled trial, the rate of death in drug-treated patients
was about 4.5%, compared to a rate of about 2.6% in the placebo group.
Although the causes of death were varied, most of the deaths appeared to
be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g.,
pneumonia) in nature. Observational studies suggest that, similar to atypical
antipsychotic drugs, treatment with conventional antipsychotic drugs may
increase mortality. The extent to which the findings of increased mortality in
observational studies may be attributed to the antipsychotic drug as opposed
to some characteristic(s) of the patients is not clear. RISPERDAL CONSTA® is
not approved for the treatment of patients with dementia-related psychosis.

Contraindications: RISPERDAL CONSTA® is contraindicated in patients with
a known hypersensitivity to risperidone, paliperidone, or to any excipients in
RISPERDAL CONSTA®.

Cerebrovascular Adverse Events (CAEs): CAEs (e.g., stroke, transient ischemia
attacks), including fatalities, were reported in placebo-controlled trials in elderly
patients with dementia-related psychosis taking oral risperidone. The incidence
of CAEs was significantly higher than with placebo. RISPERDAL CONSTA® is not
approved for the treatment of patients with dementia-related psychosis.

Please see Important Safety Information for RISPERDAL CONSTA® on pages 26 to 28 and full
Prescribing Information for RISPERDAL CONSTA®, including Boxed WARNING.
IS YOUR PATIENT WITH SCHIZOPHRENIA ALREADY TAKING INVEGA SUSTENNA®?

Use the next section to find out how to begin the transition to INVEGA TRINZA® (paliperidone palmitate) from INVEGA SUSTENNA®
INITIATING INVEGA TRINZA®
(paliperidone palmitate) TREATMENT

Start patients on a seamless dosing pathway to INVEGA TRINZA® after initiating stabilization with INVEGA SUSTENNA® (paliperidone palmitate) today1*

1. INVEGA TRINZA® is to be used only after the 1-month paliperidone palmitate extended-release injectable suspension (INVEGA SUSTENNA®) has been established as adequate treatment for at least 4 months1*

2. In order to establish a consistent maintenance dose, it is recommended that the last 2 doses of INVEGA SUSTENNA® be the same dosage strength before starting INVEGA TRINZA®1

3. For those who have not taken oral paliperidone, oral risperidone, or injectable risperidone previously, establish tolerability with oral paliperidone or oral risperidone before starting INVEGA SUSTENNA®2

*Based on your evaluation of the patient’s response.

<table>
<thead>
<tr>
<th>INVEGA TRINZA® DOSES FOR ADULT PATIENTS ADEQUATELY TREATED WITH INVEGA SUSTENNA®††</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>If the last INVEGA SUSTENNA® dose was:</td>
<td>Initiate INVEGA TRINZA® at the following dose:</td>
</tr>
<tr>
<td>78 mg</td>
<td>273 mg</td>
</tr>
<tr>
<td>117 mg</td>
<td>410 mg</td>
</tr>
<tr>
<td>156 mg</td>
<td>546 mg</td>
</tr>
<tr>
<td>234 mg</td>
<td>819 mg</td>
</tr>
</tbody>
</table>

Arrows illustrate the corresponding dose conversion from INVEGA SUSTENNA® to INVEGA TRINZA®.

†Conversion from the INVEGA SUSTENNA® 39-mg dose was not studied.

When patients are ready to transition to INVEGA TRINZA®1

1. Following the initial INVEGA TRINZA® dose, INVEGA TRINZA® should be administered once every 3 months

2. Between doses, patients can maintain scheduled treatment plans and routine interactions with their treatment team

Adjusting doses1

1. If needed, dose adjustment can be made every 3 months in increments within the range of 273 mg to 819 mg based on tolerability or efficacy

- Due to the long-acting nature of INVEGA TRINZA®, the patient’s response to an adjusted dose may not be apparent for several months
ADDRESSING MISSED DOSES

What to do when a dose is missed

INVEGA TRINZA® is administered once every 3 months. Missing doses should be avoided.

<table>
<thead>
<tr>
<th>TIME SINCE LAST INJECTION</th>
<th>ACTION STEPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early or late by 2 weeks</td>
<td>Patients may be given the injection ±2 weeks from their scheduled 3-month dose.</td>
</tr>
<tr>
<td>Longer than 3½ months but less than 4 months</td>
<td>Previous dose should be administered as soon as possible, then continue with 3-month injections.</td>
</tr>
<tr>
<td>4 months up to and including 9 months</td>
<td>Do not administer the next dose, but use the reinitiation table below.</td>
</tr>
</tbody>
</table>

Reinitiation Regimen After Missing 4 Months to 9 Months of INVEGA TRINZA®

<table>
<thead>
<tr>
<th>If the last dose of INVEGA TRINZA® was:</th>
<th>Administer INVEGA SUSTENNA® (2 doses, 1 week apart, into deltoid muscle)</th>
<th>Then administer INVEGA TRINZA® (into deltoid or gluteal muscle)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>Day 8</td>
<td>1 month after day 8</td>
</tr>
<tr>
<td>273 mg</td>
<td>78 mg</td>
<td>273 mg</td>
</tr>
<tr>
<td>410 mg</td>
<td>117 mg</td>
<td>410 mg</td>
</tr>
<tr>
<td>546 mg</td>
<td>156 mg</td>
<td>546 mg</td>
</tr>
<tr>
<td>819 mg</td>
<td>156 mg</td>
<td>819 mg</td>
</tr>
</tbody>
</table>

Arrows illustrate reinitiation regimen of INVEGA SUSTENNA® after missing 4 months to 9 months of INVEGA TRINZA®.

IMPORTANT SAFETY INFORMATION for INVEGA TRINZA® and INVEGA SUSTENNA®

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.

Please see Important Safety Information for INVEGA TRINZA® and INVEGA SUSTENNA® on pages 20 to 22 and full Prescribing Information for INVEGA TRINZA®, including Boxed WARNING, and full Prescribing Information for INVEGA SUSTENNA®, including Boxed WARNING.
DOSING CONSIDERATIONS FOR INVEGA TRINZA® (paliperidone palmitate)

Dosing adjustment in renal impairment

• INVEGA TRINZA® has not been systematically studied in patients with renal impairment

Mild renal impairment (creatinine clearance ≥50 mL/min to <80 mL/min)†

• For patients with mild renal impairment, adjust dosage and stabilize the patient using the 1-month paliperidone palmitate extended-release injectable suspension, then transition to INVEGA TRINZA®

Moderate or severe renal impairment (creatinine clearance <50 mL/min)†

• INVEGA TRINZA® is not recommended in patients with moderate or severe renal impairment

*For INVEGA SUSTENNA® (paliperidone palmitate) dosing considerations, please see enclosed full Prescribing Information for INVEGA SUSTENNA®.

†Cockcroft-Gault formula.

IMPORTANT SAFETY INFORMATION for INVEGA TRINZA® and INVEGA SUSTENNA®

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.

Please see Important Safety Information for INVEGA TRINZA® and INVEGA SUSTENNA® on pages 20 to 22 and full Prescribing Information for INVEGA TRINZA®, including Boxed WARNING, and full Prescribing Information for INVEGA SUSTENNA®, including Boxed WARNING.
DOSE PACK CONTENTS

Each kit contains:

- A prefilled syringe
- 2 thin wall safety needles
  - 22G × 1"  
  - 22G × 1½"

Thin wall safety needles are designed to be used with INVEGA TRINZA®. Therefore, it is important to only use the needles provided in the INVEGA TRINZA® kit.

Store at room temperature (20°C to 25°C [68°F to 77°F])
- No need for refrigeration
IMPORTANT

• INVEGA TRINZA® (paliperidone palmitate) should be administered by a healthcare professional as a single injection. DO NOT divide dose into multiple injections.
• INVEGA TRINZA® is intended for intramuscular use only. Inject slowly, deep into the muscle, taking care to avoid injection into a blood vessel.
• Read complete instructions prior to use.
• INVEGA TRINZA® should be administered once every 3 months.
• Peel off tab label from the syringe and place in patient record.
• INVEGA TRINZA® requires longer and more vigorous shaking than INVEGA SUSTENNA® (1-month paliperidone palmitate extended-release injectable suspension). Shake the syringe vigorously, with the syringe tip pointing up, for at least 15 seconds within 5 minutes prior to administration.

IMPORTANT SAFETY INFORMATION for INVEGA TRINZA® and INVEGA SUSTENNA®

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.

Please see Important Safety Information for INVEGA TRINZA® and INVEGA SUSTENNA® on pages 20 to 22 and full Prescribing Information for INVEGA TRINZA®, including Boxed WARNING, and full Prescribing Information for INVEGA SUSTENNA®, including Boxed WARNING.
**ADMINISTRATION INFORMATION FOR INVEGA TRINZA®**

- Parenteral drug products should be inspected visually for foreign matter and discoloration prior to administration. **It is important to shake the syringe vigorously** for at least 15 seconds to ensure a homogeneous suspension. **Inject INVEGA TRINZA® within 5 minutes of shaking vigorously.**

- In the event of an incompletely administered dose, do **not** reinject the dose remaining in the syringe and do **not** administer another dose of INVEGA TRINZA®. Closely monitor and treat the patient with oral supplementation as clinically appropriate until the next scheduled 3-month injection of INVEGA TRINZA®.

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### Select needle

Needle selection is determined by injection area and patient weight.

- **If administering a deltoid injection**
  - If patient weighs: Less than 90 kg
    - Pink hub:
      - **22G × 1"**
    - 90 kg or more
      - Yellow hub:
        - **22G × 1½"**

- **If administering a gluteal injection**
  - If patient weighs: Less than 90 kg
    - Yellow hub:
      - **22G × 1½"**
  - 90 kg or more
    - Yellow hub:
      - **22G × 1½"**

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*Immediately discard the unused needle in an approved Sharps Container. Do not save for future use.*

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*For INVEGA SUSTENNA® (paliperidone palmitate) administration information, please see full Prescribing Information for INVEGA SUSTENNA®, including Boxed WARNING, and Instructions for Use.*
2 Prepare for injection

SHAKE VIGOROUSLY for at least 15 seconds

With the syringe tip pointing up, SHAKE VIGOROUSLY with a loose wrist for at least 15 seconds to ensure a homogeneous suspension.

NOTE: This medication requires longer and more vigorous shaking than the 1-month paliperidone palmitate extended-release injectable suspension.

Proceed to the next step immediately after shaking. If more than 5 minutes pass before injection, shake vigorously, with the syringe tip pointing up, again for at least 15 seconds to resuspend the medication.

Please see Important Safety Information for INVEGA TRINZA® and INVEGA SUSTENNA® on pages 20 to 22 and full Prescribing Information for INVEGA TRINZA®, including Boxed WARNING, and full Prescribing Information for INVEGA SUSTENNA®, including Boxed WARNING.
Check suspension
After shaking the syringe for at least 15 seconds, check the liquid in the viewing window.
The suspension should appear uniform and milky white in color.
It is also normal to see small air bubbles.

Open needle pouch and remove cap
First, open needle pouch by peeling the cover back halfway. Place on a clean surface.
Then, holding the syringe upright, twist and pull the rubber cap to remove.

Grasp needle pouch
Fold back needle cover and plastic tray. Then, firmly grasp the needle sheath through the pouch, as shown.
Attach needle
With your other hand, hold the syringe by the Luer connection and attach it to the safety needle with a gentle clockwise twisting motion.
Do not remove the pouch until the syringe and needle are securely attached.

Remove needle sheath
Pull the needle sheath away from the needle in a straight motion.
Do not twist the sheath, as this may loosen the needle from the syringe.

Remove air bubbles
Hold the syringe upright and tap gently to make any air bubbles rise to the top.
Remove air by pressing the plunger rod upward carefully until a drop of liquid comes out of the needle tip.

Please see Important Safety Information for INVEGA TRINZA® and INVEGA SUSTENNA® on pages 20 to 22 and full Prescribing Information for INVEGA TRINZA®, including Boxed WARNING, and full Prescribing Information for INVEGA SUSTENNA®, including Boxed WARNING.
3 Inject

**Inject dose**
Slowly inject the entire contents of the syringe intramuscularly, deep into the selected deltoid or gluteal muscle.
**Do not administer by any other route.**

4 After injection

**Secure needle**
After the injection is complete, use your thumb or a flat surface to secure the needle in the safety device.
The needle is secure when a “click” sound is heard.

**Dispose properly**
Dispose of the syringe and unused needle in an approved Sharps Container.

⚠️ Thin wall safety needles are designed specifically for use with INVEGA TRINZA® (paliperidone palmitate). Unused needle should be discarded and not saved for future use.

INVEGA TRINZA®
Paliperidone Palmitate
273 mg, 410 mg, 546 mg, 819 mg

ADMINISTRATION
IMPORTANT SAFETY INFORMATION for INVEGA TRINZA® and INVEGA SUSTENNA®

INDICATION
INVEGA TRINZA® (paliperidone palmitate) a 3-month injection, is an atypical antipsychotic indicated for the treatment of schizophrenia in patients after they have been adequately treated with INVEGA SUSTENNA® (1-month paliperidone palmitate) for at least four months.

INVEGA SUSTENNA® (paliperidone palmitate) is an atypical antipsychotic indicated for the treatment of schizophrenia.

IMPORTANT SAFETY INFORMATION

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 TRINZA® and INVEGA SUSTENNA® are 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 at a higher incidence in elderly patients with dementia-related psychosis taking risperidone, aripiprazole, and olanzapine compared to placebo. No studies have been conducted with oral paliperidone, INVEGA SUSTENNA®, or INVEGA TRINZA® in elderly patients with dementia. These medications are 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.

Please see full Prescribing Information for INVEGA TRINZA®, including Boxed WARNING, and full Prescribing Information for INVEGA SUSTENNA®, including Boxed WARNING.
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 TRINZA® and INVEGA SUSTENNA® may induce orthostatic hypotension in some patients due to its alpha-adrenergic blocking activity. INVEGA TRINZA® and 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 TRINZA® and 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 INVEGA TRINZA® and INVEGA SUSTENNA®. In patients with a history of clinically significant low white blood cell count (WBC)/absolute neutrophil count (ANC) or drug-induced leukopenia/neutropenia, perform a complete blood count frequently during the first few months of therapy. Consider
discontinuing INVEGA TRINZA® and INVEGA SUSTENNA® at the first sign of a clinically significant decline in WBC in the absence of other causative factors. Monitor patients with clinically significant neutropenia for fever or other symptoms or signs of infection and treat promptly if such symptoms or signs occur. Discontinue INVEGA TRINZA® and INVEGA SUSTENNA® in patients with severe neutropenia (absolute neutrophil count <1000/mm³) and follow their WBC until recovery.

Hyperprolactinemia: As with other drugs that antagonize dopamine D₂ receptors, INVEGA TRINZA® and INVEGA SUSTENNA® elevate 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 TRINZA® and INVEGA SUSTENNA®. INVEGA TRINZA® and INVEGA SUSTENNA® have 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 TRINZA® and INVEGA SUSTENNA® do not adversely affect them.

Seizures: INVEGA TRINZA® and 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 using only the needles provided in the INVEGA TRINZA® or INVEGA SUSTENNA® kits. Care should be taken to avoid inadvertent injection into a blood vessel.

Drug Interactions: Strong CYP3A4/P-glycoprotein (P-gp) inducers: Avoid using a strong inducer of CYP3A4 and/or P-gp (e.g., carbamazepine, rifampin, St John’s Wort) during a dosing interval for INVEGA TRINZA® or INVEGA SUSTENNA®. If administering a strong inducer is necessary, consider managing the patient using paliperidone extended-release tablets.

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 TRINZA® and INVEGA SUSTENNA®.

Commonly Observed Adverse Reactions for INVEGA TRINZA®: The most common adverse reactions (incidence ≥ 5% and occurring at least twice as often as placebo) were injection site reaction, weight increased, headache, upper respiratory tract infection, akathisia and parkinsonism.

Commonly Observed Adverse Reactions for INVEGA SUSTENNA®: The most common adverse reactions in clinical trials in patients with schizophrenia (incidence ≥ 5% and occurring at least twice as often as placebo) were injection site reactions, somnolence/sedation, dizziness, akathisia and extrapyramidal disorder.

Please see full Prescribing Information for INVEGA TRINZA®, including Boxed WARNING, and full Prescribing Information for INVEGA SUSTENNA®, including Boxed WARNING.
IMPORTANT SAFETY INFORMATION for INVEGA®

INDICATION
INVEGA® (paliperidone) extended-release tablets are indicated for the treatment of schizophrenia in adults. The efficacy of INVEGA® in schizophrenia was established in three 6-week trials in adults, as well as one maintenance trial in adults.

IMPORTANT SAFETY 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. Analyses of 17 placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (eg, heart failure, sudden death) or infectious (eg, pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear. INVEGA® is not approved for the treatment of patients with dementia-related psychosis.

Contraindications: Paliperidone is contraindicated in patients with a known hypersensitivity to paliperidone, risperidone, or to any excipients in INVEGA®.

Cerebrovascular Adverse Events (CAEs): CAEs (eg, stroke, transient ischemia 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 CAEs was significantly higher than with placebo. INVEGA® 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.

Please see full Prescribing Information for INVEGA®, including Boxed WARNING.
IMPORTANT SAFETY INFORMATION for INVEGA® (cont’d)

QT Prolongation: Paliperidone causes a modest increase in the corrected QT (QTc) interval. Avoid the use of drugs that also increase QT interval and in patients with risk factors for prolonged QT 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 torsade 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 women 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. The 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 – Hyperglycemia, some cases extreme and associated with ketoacidosis, hyperosmolar coma, or death has been reported in patients treated with atypical antipsychotics (APS), including INVEGA® (paliperidone). 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 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 anti-diabetic treatment despite discontinuation of the suspect drug.
- Dyslipidemia – Undesirable alterations in lipids 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.

Hyperprolactinemia: As with other drugs that antagonize dopamine D₂ receptors, INVEGA® 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.

Gastrointestinal: INVEGA® should ordinarily not be administered to patients with pre-existing severe gastrointestinal narrowing. Rare instances of obstructive symptoms have been reported in patients with known strictures taking non-deformable formulations. INVEGA® should only be used in patients who are able to swallow the tablet whole.

Please see full Prescribing Information for INVEGA®, including Boxed WARNING.
Orthostatic Hypotension and Syncope: INVEGA® may induce orthostatic hypotension in some patients due to its alpha-blocking activity. INVEGA® should be used with caution in patients with known cardiovascular disease (e.g., heart failure, history of MI or ischemia, conduction abnormalities), cerebrovascular disease or conditions that would predispose patients to hypotension (e.g., dehydration, hypovolemia, treatment with anti-hypertensive medications). Monitoring should be considered in patients who are vulnerable to hypotension.

Falls: Somnolence, postural hypotension, motor and sensory instability have been reported with the use of antipsychotics, including INVEGA®, 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® 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® and have their WBC followed until recovery.

Potential for Cognitive and Motor Impairment: Somnolence was reported in subjects treated with INVEGA®. INVEGA® 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® does not adversely affect them.

Seizures: INVEGA® 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.

Suicide: The possibility of suicide attempt is inherent in psychotic illnesses. Close supervision of high-risk patients should accompany drug therapy. Prescriptions should be written for the smallest quantity of tablets to reduce the risk of overdose.

Drug Interactions: Strong CYP3A4/P-glycoprotein (P-gp) inducers: It may be necessary to increase the dose of INVEGA® 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®.

Commonly Observed Adverse Reactions: The most commonly observed adverse reactions in clinical trials occurring at an incidence of ≥5% and at least 2 times placebo in the treatment of schizophrenia were: Adults – extrapyramidal symptoms, tachycardia, and akathisia.
IMPORTANT SAFETY INFORMATION for RISPERDAL CONSTA®

INDICATION
RISPERDAL CONSTA® (risperidone) long-acting injection is indicated for the treatment of schizophrenia.

IMPORTANT SAFETY 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. Analyses of 17 placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear. RISPERDAL CONSTA® is not approved for the treatment of patients with dementia-related psychosis.

Contraindications: RISPERDAL CONSTA® is contraindicated in patients with a known hypersensitivity to risperidone, paliperidone, or to any excipients in RISPERDAL CONSTA®.

Cerebrovascular Adverse Events (CAEs): CAEs (e.g., stroke, transient ischemia attacks), including fatalities, were reported in placebo-controlled trials in elderly patients with dementia-related psychosis taking oral risperidone. The incidence of CAEs was significantly higher than with placebo. RISPERDAL CONSTA® 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. 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.

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 women patients appeared to

Please see full Prescribing Information for RISPERDAL CONSTA®, including Boxed WARNING.
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, some cases extreme and associated with ketoacidosis, hyperosmolar coma or death have been reported in patients treated with atypical antipsychotics (APS), including RISPERDAL CONSTA®. 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 should also undergo fasting blood glucose testing. All patients treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia. Monitor glucose regularly in patients with diabetes or at risk for diabetes. 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.

Hyperprolactinemia: As with other drugs that antagonize dopamine D₂ receptors, risperidone elevates prolactin levels and the elevation persists during chronic administration. Risperidone is associated with higher levels of prolactin elevation than other antipsychotic agents.

**Orthostatic Hypotension and Syncope:** RISPERDAL CONSTA® may induce orthostatic hypotension associated with dizziness, tachycardia, and in some patients, syncope, especially during the initial dose-titration period. RISPERDAL CONSTA® should be used with caution in patients with known cardiovascular disease (e.g., heart failure, history of MI or ischemia, conduction abnormalities), cerebrovascular disease or conditions that would predispose patients to hypotension (e.g., dehydration, hypovolemia) and additionally elderly patients with renal or hepatic impairment. 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 RISPERDAL CONSTA®, 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.
IMPORTANT SAFETY INFORMATION for RISPERDAL CONSTA® (cont’d)

Leukopenia, Neutropenia and Agranulocytosis have been reported with antipsychotics, including RISPERDAL CONSTA®. 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 RISPERDAL CONSTA® (risperidone) 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 RISPERDAL CONSTA® and have their WBC followed until recovery.

Potential for Cognitive and Motor Impairment: Somnolence was reported in multiple trials in subjects treated with RISPERDAL CONSTA®. Since RISPERDAL CONSTA® has the potential to impair judgment, thinking, or motor skills, patients should be cautioned about operating hazardous machinery, including motor vehicles, until they are reasonably certain that RISPERDAL CONSTA® does not adversely affect them.

Seizures: RISPERDAL CONSTA® should be used cautiously in patients with a history of seizures.

Dysphagia: Esophageal dysmotility and aspiration have been associated with antipsychotic drug use. Aspiration pneumonia is a common cause of morbidity and mortality in patients with advanced Alzheimer’s dementia. Use cautiously in patients at risk for aspiration pneumonia.

Priapism has been reported. Severe priapism may require surgical intervention.

Thrombotic Thrombocytopenic Purpura (TTP) has been reported.

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

Suicide: The possibility of suicide attempt is inherent in schizophrenia or bipolar disorder. Close supervision of high-risk patients should accompany drug therapy.

Increased sensitivity in patients with Parkinson’s disease or those with dementia with Lewy bodies has been reported. Manifestations and features are consistent with NMS.

Use RISPERDAL CONSTA® with caution in patients with conditions and medical conditions that could affect metabolism or hemodynamic responses (e.g., recent myocardial infarction or unstable cardiac disease).

Commonly Observed Adverse Reactions for RISPERDAL CONSTA®: The most common adverse reactions in clinical trials in patients with schizophrenia (≥5%) were headache, Parkinsonism, dizziness, akathisia, fatigue, constipation, dyspepsia, sedation, weight increase, pain in extremities, and dry mouth.

Please see full Prescribing Information for RISPERDAL CONSTA®, including Boxed WARNING.
A video demonstration of the INVEGA TRINZA® (paliperidone palmitate) Instructions for Use, which includes Dosing and Administration information, can be found at invegatrinzahcp.com

Please call 1-800-JANSSEN (1-800-526-7736) Monday through Friday: 9:00 AM to 8:00 PM ET


Please see Important Safety Information for INVEGA TRINZA® and INVEGA SUSTENNA® on pages 20 to 22 and full Prescribing Information for INVEGA TRINZA®, including Boxed WARNING, and full Prescribing Information for INVEGA SUSTENNA®, including Boxed WARNING.