INVEGA TRINZA™ Fact Sheet

Overview

INVEGA TRINZA™ (three-month paliperidone palmitate) long-acting medication is approved by the U.S. Food and Drug Administration (FDA) to treat schizophrenia in patients after they have been adequately treated with INVEGA SUSTENNA® (one-month paliperidone palmitate) for at least four months. It is the first and only medication for schizophrenia that is administered four times a year, providing the longest dosing interval available. In a long-term maintenance trial, 93 percent of patients treated with INVEGA TRINZA™ did not experience a significant return of schizophrenia symptoms. With this new treatment option, healthcare providers can give patients greater independence by enabling them to focus less on taking their medication and more on other aspects of their treatment plan.

Indication

INVEGA TRINZA™, a three-month paliperidone palmitate injection, is an atypical antipsychotic indicated for the treatment of schizophrenia. INVEGA TRINZA™ can only be used after patients have been adequately treated with INVEGA SUSTENNA® for at least four months.

The FDA granted the INVEGA TRINZA™ New Drug Application priority review status, a designation reserved for drugs that, if approved, would offer significant improvement in the treatment of serious conditions. Janssen plans filings for three-month paliperidone palmitate in many markets outside of the U.S. later this year.

The one-month formulation of paliperidone palmitate INVEGA SUSTENNA® was approved by the U.S. FDA in July 2009 as the first once-monthly atypical long-acting injection to treat schizophrenia and is now approved in more than 80 countries. In 2014 the FDA approved INVEGA SUSTENNA® to treat schizoaffective disorder, making it the first and only once-monthly medication to treat the condition.

Dosing and Administration

INVEGA TRINZA™ is the first and only medication for schizophrenia to provide sustained symptom control with a single dose when administered every three months, with a dosing interval of that can be measured in seasons, not days. Before starting INVEGA TRINZA™, patients must be adequately treated with INVEGA SUSTENNA® for at least four months, after
which they can be seamlessly transitioned to INVEGA TRINZA™. INVEGA TRINZA™ may be an option for patients whose treatment plan includes a goal of pursuing greater independence, beyond just short-term symptom control.

**Key Clinical Data**

The FDA approval of INVEGA TRINZA™ was based on a long-term maintenance trial of paliperidone palmitate three-month injection. The study, which included more than 500 patients, evaluated the efficacy of INVEGA TRINZA™ compared with placebo in delaying time to first occurrence of relapse of symptoms of schizophrenia. During the trial, 93 percent of patients treated with INVEGA TRINZA™ did not experience a significant return of schizophrenia symptoms.

The long-term maintenance trial consisted of three distinct phases. All patients were treated for 17 weeks with INVEGA SUSTENNA® during an open-label stabilization phase, and then a single dose of INVEGA TRINZA™ during an open-label maintenance phase for 12 weeks. This phase was followed by patients being randomized to receive either a dose of INVEGA TRINZA™ or placebo once every 3 months in a double-blind phase. The mean duration of exposure during the double-blind phase was 175 days in the INVEGA TRINZA™ group and 150 days in the placebo group.

During the double-blind phase of the trial, the median time to relapse, or estimated point when half of the patients relapsed, in the placebo arm was approximately nine months (274 days). The median time to relapse in the INVEGA TRINZA™ arm could not be estimated due to low percentage (7.4%) of subjects with relapse.

Based on positive efficacy, Janssen concluded this study early following the recommendation of an Independent Data Monitoring Committee (IDMC).

Relapse was defined as worsening schizophrenia symptoms, such as at least 25% increase in PANSS total score\(^1\), increase in distinct PANSS item scores, psychiatric hospitalization, deliberate self-injury or violent behavior, or suicidal or homicidal ideation.

\(^1\) Defined as a 25% increase for 2 consecutive assessments between 3 and 7 days apart for patients scoring >40 at randomization or a 10-point increase for patients scoring ≤40 at randomization.
The most common adverse reactions (incidence greater than or equal to 5% and occurring at least twice as often as placebo) were injection site reaction, increased weight, headache, upper respiratory tract infection, akathisia, and parkinsonism.

**How It Works**

The gradual release characteristics and dosing regimen of INVEGA TRINZA™ result in sustained therapeutic concentrations over three months. INVEGA TRINZA™ utilizes Alkermes’ proprietary NanoCrystal® technology, which enables solubility of poorly water-soluble compounds. Once in the body, these particles slowly dissolve, gradually releasing a controlled amount of medication consistently over time.

**Important Safety Information**

**INDICATION**
INVEGA TRINZA™ (3-month paliperidone palmitate) is a prescription medicine given by injection every 3 months by a healthcare professional and used to treat schizophrenia. INVEGA TRINZA™ is used in people who have been treated with INVEGA SUSTENNA® (1-month paliperidone palmitate) for at least 4 months.

**IMPORTANT SAFETY INFORMATION**

INVEGA TRINZA™ can cause serious side effects, including an increased risk of death in elderly people who are confused, have memory loss, and have lost touch with reality (dementia-related psychosis). INVEGA TRINZA™ is not approved for treating dementia-related psychosis.

Do not receive INVEGA TRINZA™ if you are allergic to paliperidone palmitate, risperidone, or any of the ingredients in INVEGA TRINZA™. See end of the Patient Information leaflet in the full Prescribing Information for a complete list of INVEGA TRINZA™ ingredients.

**Before you receive INVEGA TRINZA™,** tell your healthcare provider about all your medical conditions, including if you:

- have had Neuroleptic Malignant Syndrome (NMS)
- have or have had heart problems, including a heart attack, heart failure, abnormal heart rhythm, or long QT syndrome
• have or have had low levels of potassium or magnesium in your blood
• have or have had uncontrolled movements of your tongue, face, mouth, or jaw (tardive dyskinesia)
• have or have had kidney or liver problems
• have diabetes or have a family history of diabetes
• have had a low white blood cell count
• have had problems with dizziness or fainting or are being treated for high blood pressure
• have or have had seizures or epilepsy
• have any other medical conditions
• are pregnant or plan to become pregnant. It is not known if INVEGA TRINZA™ will harm your unborn baby
  o If you become pregnant while taking INVEGA TRINZA™, talk to your healthcare provider about registering with the National Pregnancy Registry for Atypical Antipsychotics. You can register by calling 1-866-961-2388 or visit http://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry
  o Infants born to women who are treated with INVEGA TRINZA™ may have withdrawal symptoms or other symptoms such as tremors, muscle spasms, abnormal movement of arms and legs, and twitching of eyes
• are breastfeeding or plan to breastfeed. INVEGA TRINZA™ can pass into your breast milk and may harm your baby. You and your healthcare provider should decide if you will receive INVEGA TRINZA™ or breastfeed. You should not do both

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Know the medicines you take. Keep a list of them to show to your healthcare provider or pharmacist when you get a new medicine.

What should I avoid while receiving INVEGA TRINZA™?
• INVEGA TRINZA™ may affect your ability to make decisions, think clearly, or react quickly. Do not drive, operate heavy machinery, or do other dangerous activities until you know how INVEGA TRINZA™ affects you
• avoid getting overheated or dehydrated
INVEGA TRINZA™ may cause serious side effects, including:

- **stroke in elderly people (cerebrovascular problems) that can lead to death**

- **Neuroleptic Malignant Syndrome (NMS).** NMS is a rare but very serious problem that can happen in people who receive INVEGA TRINZA™. NMS can cause death and must be treated in a hospital. Call your healthcare provider right away if you become severely ill and have any of these symptoms: high fever; severe muscle stiffness; confusion; loss of consciousness; changes in your breathing, heartbeat, and blood pressure

- **problems with your heartbeat.** These heart problems can cause death. Call your healthcare provider right away if you have any of these symptoms: passing out or feeling like you will pass out, dizziness, or feeling as if your heart is pounding or missing beats

- **uncontrolled movements of your tongue, face, mouth, or jaw (tardive dyskinesia)**

- **metabolic changes.** Metabolic changes may include high blood sugar (hyperglycemia), diabetes mellitus and changes in the fat levels in your blood (dyslipidemia), and weight gain

- **low blood pressure and fainting**

- **changes in your blood cell counts**

- **high level of prolactin in your blood (hyperprolactinemia).** INVEGA TRINZA™ may cause a rise in the blood levels of a hormone called prolactin (hyperprolactinemia) that may cause side effects including missed menstrual periods, leakage of milk from the breasts, development of breasts in men, or problems with erection

- **problems thinking clearly and moving your body**

- **seizures**

- **difficulty swallowing that can cause food or liquid to get into your lungs**

- **prolonged or painful erection lasting more than 4 hours.** Call your healthcare provider or go to your nearest emergency room right away if you have an erection that lasts more than 4 hours

- **problems with control of your body temperature, especially when you exercise a lot or spend time doing things that make you warm. It is important for you to drink water to avoid dehydration**

- **Call your doctor right away if you start thinking about suicide or wanting to hurt yourself**
The most common side effects of INVEGA TRINZA™ include: injection site reactions, weight gain, headache, upper respiratory tract infections, feeling restlessness or difficulty sitting still, slow movements, tremors, stiffness, and shuffling walk.

Tell your healthcare provider if you have any side effect that bothers you or does not go away. These are not all the possible side effects of INVEGA TRINZA™. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects of prescription drugs to the FDA at 1-800-FDA-1088.

General information about the safe and effective use of INVEGA TRINZA™.
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use INVEGA TRINZA™ for a condition for which it was not prescribed. Do not give INVEGA TRINZA™ to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about INVEGA TRINZA™ that is written for health professionals.

The Patient Information leaflet summarizes the most important information about INVEGA TRINZA™. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for more information that is written for healthcare professionals. For more information, go to www.invegatrinzahcp.com or call 1-800-526-7736.

About INVEGA SUSTENNA®

INDICATIONS
INVEGA SUSTENNA® (In-VEY-guh Suss-TEN-uh) (paliperidone palmitate) Extended-Release Injectable Suspension is a prescription medicine given by injection by a healthcare professional. INVEGA SUSTENNA® is used for schizoaffective disorder either alone or in combination with other medicines such as mood stabilizers or antidepressants and is used to treat schizophrenia.

INVEGA SUSTENNA® can cause serious side effects, including an increased risk of death in elderly people who are confused, have memory loss, and have lost touch with reality (dementia-related psychosis). INVEGA SUSTENNA® is not approved for treating dementia-related psychosis.

Do not receive INVEGA SUSTENNA® if you are allergic to paliperidone, risperidone, or any of the ingredients in INVEGA SUSTENNA®. See end of the Patient Information leaflet in the full Prescribing Information for a complete list of INVEGA SUSTENNA® ingredients.

Before you receive INVEGA SUSTENNA®, tell your healthcare provider about all your medical conditions, including if you:

• have had Neuroleptic Malignant Syndrome (NMS)
• have or have had heart problems, including a heart attack, heart failure, abnormal heart rhythm, or long QT syndrome
• have or have had low levels of potassium or magnesium in your blood
• have or have had uncontrolled movements of your tongue, face, mouth, or jaw (tardive dyskinesia)
• have or have had kidney or liver problems
• have diabetes or have a family history of diabetes
• have had a low white blood cell count
• have had problems with dizziness or fainting or are being treated for high blood pressure
• have or have had seizures or epilepsy
• have any other medical conditions
• are pregnant or plan to become pregnant. It is not known if INVEGA SUSTENNA® will harm your unborn baby
• are breastfeeding or plan to breastfeed. INVEGA SUSTENNA® can pass into your breast milk and may harm your baby. You and your healthcare provider should decide if you will receive INVEGA SUSTENNA® or breastfeed. You should not do both

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Know the medicines you take. Keep a list of them to show to your healthcare provider or pharmacist when you get a new medicine.

What should I avoid while receiving INVEGA SUSTENNA®?
• INVEGA SUSTENNA® may affect your ability to make decisions, think clearly, or react quickly. Do not drive, operate heavy machinery, or do other dangerous activities until you know how INVEGA SUSTENNA® affects you
• avoid getting overheated or dehydrated

INVEGA SUSTENNA® may cause serious side effects, including:
• stroke in elderly people (cerebrovascular problems) that can lead to death
• Neuroleptic Malignant Syndrome (NMS). NMS is a rare but very serious problem that can happen in people who receive INVEGA SUSTENNA®. NMS can cause death and must be treated in a hospital. Call your healthcare provider right away if you become severely ill and
have any of these symptoms: high fever; severe muscle stiffness; confusion; loss of consciousness; changes in your breathing, heartbeat, and blood pressure

- **problems with your heartbeat.** Heart problems can cause death. Call your healthcare provider right away if you have any of these symptoms: passing out or feeling like you will pass out; dizziness; or feeling as if your heart is pounding or missing beats

- **uncontrolled movements of your tongue, face, mouth, or jaw (tardive dyskinesia)**

- **metabolic changes.** Metabolic changes may include high blood sugar (hyperglycemia), diabetes mellitus and changes in the fat levels in your blood (dyslipidemia), and weight gain

- **low blood pressure and fainting**

- **changes in your blood cell counts**

- **high level of prolactin in your blood (hyperprolactinemia).** INVEGA SUSTENNA® may cause a rise in the blood levels of a hormone called prolactin (hyperprolactinemia) that may cause side effects including missed menstrual periods, leakage of milk from the breasts, development of breasts in men, or problems with erection

- **problems thinking clearly and moving your body**

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- **difficulty swallowing that can cause food or liquid to get into your lungs**

- **prolonged or painful erection lasting more than 4 hours.** Call your healthcare provider or go to your nearest emergency room right away if you have an erection that lasts more than 4 hours

- **problems with control of your body temperature, especially when you exercise a lot or spend time doing things that make you warm. It is important for you to drink water to avoid dehydration**

- **Call your doctor right away if you start thinking about suicide or wanting to hurt yourself**

The most common side effects of INVEGA SUSTENNA® include: injection site reactions; sleepiness or drowsiness; dizziness; feeling of inner restlessness or needing to be constantly moving; abnormal muscle movements, including tremor (shaking), shuffling, uncontrolled involuntary movements, and abnormal movements of your eyes.

Tell your healthcare provider if you have any side effect that bothers you or does not go away. These are not all the possible side effects of INVEGA SUSTENNA®. For more information, ask your healthcare provider or pharmacist.
You are encouraged to report side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see full Prescribing Information including Boxed Warning for INVEGA SUSTENNA® (paliperidone palmitate) and INVEGA® (paliperidone) at www.JanssenCNS.com/InvegaSustenna and www.JanssenCNS.com/Invega.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding a newly approved product. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Pharmaceuticals, Inc. and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: manufacturing difficulties and delays; product efficacy or safety concerns resulting in product recalls or regulatory action; competition, including technological advances, new products and patents attained by competitors; challenges to patents; uncertainty of commercial success; changes in behavior and spending patterns or financial distress of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and description of these risks, uncertainties and other factors can be found in Johnson & Johnson’s Annual Report on Form 10-K for the fiscal year ended December 28, 2014, including in Exhibit 99 thereto, and the company’s subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies or Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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