**News Release**

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# Janssen Announces U.S. FDA Approval of INVEGA HAFYERA™ (6-month paliperidone palmitate), First and Only Twice-Yearly Treatment for Adults with Schizophrenia

*INVEGA HAFYERA™ offers patients the fewest doses per year for a life less defined by schizophrenia medication*

*Phase 3 non-inferiority study results showed over 92% of participants were relapse-free at 12 months*

*Approval is backed by nearly two decades of proven efficacy and safety of Janssen's long-acting injectable portfolio of schizophrenia medicines*

**TITUSVILLE, N.J., Sept. 1, 2021** – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced the U.S. Food and Drug Administration (FDA) has approved long-acting atypical antipsychotic

INVEGA HAFYERA™ (6-month paliperidone palmitate), the first-and-only twice-yearly injectable for the treatment of schizophrenia in adults. Before transitioning to INVEGA HAFYERA™, patients must be adequately treated with INVEGA SUSTENNA® (1-month paliperidone palmitate) for at least four months, or INVEGA TRINZA® (3-month paliperidone palmitate) for at least one 3-month injection cycle.[1]

The FDA approval of INVEGA HAFYERA™ is based on the results of a 12-month, randomized, double-blind, non-inferiority Phase 3 global study that enrolled 702 adults (ages 18-70) living with schizophrenia from 20 countries. The results showed non-inferiority of INVEGA HAFYERA™ compared to INVEGA TRINZA® on the primary endpoint of time to first relapse at the end of the 12-month period. Results found that 92.5 percent of patients treated with INVEGA HAFYERA™ and 95 percent treated with INVEGA TRINZA® were relapse-free at 12 months.[1] Relapse was defined as psychiatric hospitalization, increase in Positive and Negative Syndrome Scale [PANSS] total score, increase in individual PANSS item scores, self-injury, violent behavior, or suicidal/homicidal ideation.

The safety profile observed in the trial was consistent with previous studies of INVEGA SUSTENNA® and INVEGA TRINZA® with no new safety signals emerging.[1] The most common adverse reactions (≥5%) in the INVEGA HAFYERA™ clinical trial were upper respiratory tract infection (12%), injection site reaction (11%), weight increase (9%), headache (7%), and parkinsonism (5%).[1]

Click-to-Tweet: #BREAKINGNEWS the @US_FDA approved new long-acting injectable treatment with fewer doses a year for adult patients living with #schizophrenia. Click here to learn more: https://bit.ly/3gDSI3j

"Before I found the right treatment plan for me, my symptoms often got in the way of things that I loved to do," said Patrick, an adult living with

schizophrenia and a participant in the clinical trial. "But since my doctor introduced me to Janssen's long-acting injectable options and my symptoms are controlled, I have the clarity to focus on the present, but also the stability to plan for my future."

Click-to-Tweet: Patrick, an adult living with schizophrenia, talks about his treatment journey and how a long-acting injectable has helped him stay on track with his goals: https://bit.ly/3gDSI3j

Schizophrenia is a complex and chronic brain disorder in which the symptoms and potential for relapse (or recurrence of symptoms) can impact many aspects of a person's daily life. On average, an adult with schizophrenia experiences nine relapses in less than six years, often due to missed doses of medication.[2] Adults living with schizophrenia and their loved ones face ongoing functional, emotional, and financial burdens. In addition, patients who experience more relapses may have more hospitalizations, which can lead to higher medical costs for patients, hospital systems, and payers.

"For too long, we've accepted relapse as a normal part of living with schizophrenia, while research continues to demonstrate that stronger medication adherence means better patient outcomes," said Gustavo Alva*, M.D., DFAPA, Medical Director at ATP Clinical Research and 6-month paliperidone palmitate clinical trial investigator. "The Phase 3 trial results provide compelling evidence that 6-month paliperidone palmitate offers longer-term symptom control with the fewest doses per year, which may support greater patient adherence."

Recently, the National Council for Mental Wellbeing and the American Psychiatric Association updated their schizophrenia treatment guidance and guidelines to expand the recommended use of long-acting injectables for appropriate adult patients living with schizophrenia.[3,4,5]

INVEGA HAFYERA™ is a long-acting injectable treatment that is administered by a healthcare provider in the upper buttocks area every six months. INVEGA HAFYERA™ dissolves slowly into the bloodstream after injection, resulting in continuous treatment and symptom control over six months.[1]

"Long-acting injectable treatments offer a number of advantages compared to oral medication for schizophrenia, including relief from needing to remember to take medication daily, lower discontinuation rates, and sustained treatment over longer periods," said Bill Martin, Ph.D., Global Therapeutic Area Head, Neuroscience, Janssen Research & Development, LLC. "Today's approval enables us to rethink how we manage this chronic disease by offering patients and caregivers the potential for a life less defined by schizophrenia medication."

The Janssen U.S. portfolio of long-acting injectable treatments for adults with schizophrenia provides the most varied range of dosing options and the longest-lasting schizophrenia treatments available. Our portfolio includes RISPERDAL CONSTA® (risperidone),[6] INVEGA SUSTENNA® (1-month paliperidone palmitate),[7] INVEGA TRINZA® (3-month paliperidone palmitate),[8] and INVEGA HAFYERA™ (6-month paliperidone palmitate),[1] all of which are administered in a clinical setting by a medical professional.

"The approval of INVEGA HAFYERA™ builds on our 60-year legacy of delivering transformational medicines for adults living with schizophrenia," said Mathai Mammen, M.D., Ph.D., Global Head, Janssen Research & Development, Johnson & Johnson. "This approval further underscores our steadfast commitment to addressing critical unmet needs, including treatment adherence concerns, faced by adults living with schizophrenia."

Janssen CarePath offers a comprehensive support program that helps patients get started on INVEGA HAFYERA™ and stay on track. Janssen CarePath provides information on insurance coverage, potential out-of-

pocket costs, and treatment support, and identifies options that may help make treatment more affordable, including the Janssen CarePath Savings Program for commercially insured patients who are eligible.

**Dr. Alva has received research support from Janssen and has served as a paid consultant to the Company.*

Please click here to read the full Prescribing Information, including Boxed WARNING, for INVEGA HAFYERA™.

**INDICATION**

INVEGA HAFYERA™ is a prescription medicine given by injection by a healthcare provider 1 time every 6 months and used for the treatment of schizophrenia in adults who have been adequately treated with either:

- A 1-time-each-month paliperidone palmitate extended-release injectable suspension for at least 4 months
- A 1-time-every-3-months paliperidone palmitate extended-release injectable suspension for at least 3 months

**IMPORTANT SAFETY INFORMATION**

**What is the most important information I should know about INVEGA HAFYERA™?**

**INVEGA HAFYERA™ may cause serious side effects, including:**

- **Increased risk of death in elderly people with dementia-related psychosis.**
  INVEGA HAFYERA™ increases the risk of death in elderly people who have lost touch with reality (psychosis) due to confusion and memory loss (dementia). INVEGA HAFYERA™ is not for the treatment of people with dementia-related psychosis.

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

**Before receiving INVEGA HAFYERA™, 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 Parkinson's disease or a type of dementia called Lewy Body Dementia
- 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
- are pregnant or plan to become pregnant. It is not known if INVEGA HAFYERA™ will harm your unborn baby.
    - Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with INVEGA HAFYERA™.
    - If you become pregnant while receiving INVEGA HAFYERA™, 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/.
    - Babies born to mothers who receive INVEGA HAFYERA™ during their third trimester of pregnancy may develop agitation, low muscle tone (floppy baby syndrome), tremors, excessive sleepiness, breathing problems, and feeding problems. Tell your healthcare provider right away if your baby develops any of these symptoms.
- are breastfeeding or plan to breastfeed. INVEGA HAFYERA™ can pass into your breast milk. Talk to your healthcare provider about the best way to feed your baby during treatment with INVEGA HAFYERA™.

**Tell your healthcare provider about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

INVEGA HAFYERA™ and other medicines may affect each other causing possible serious side effects. INVEGA HAFYERA™ may affect the way other

medicines work, and other medicines may affect how INVEGA HAFYERA™ works.

Your healthcare provider can tell you if it is safe to receive INVEGA HAFYERA™ with your other medicines. Do not start or stop any medicines during treatment with INVEGA HAFYERA™ without talking to your healthcare provider first.

Know the medicines you take. Keep a list of them to show to your healthcare provider or pharmacist when you get a new medicine.

**How will I receive INVEGA HAFYERA™?**

- Follow your INVEGA HAFYERA™ treatment schedule exactly as your healthcare provider tells you to.
- Your healthcare provider will tell you how much INVEGA HAFYERA™ you will receive and when you will receive it.
- INVEGA HAFYERA™ is given as an injection by your healthcare provider into the muscle (intramuscularly) of your buttocks, 1 time every 6 months.

**What should I avoid while receiving INVEGA HAFYERA™?**

- Do not drive, operate heavy machinery, or do other dangerous activities until you know how INVEGA HAFYERA™ affects you. INVEGA HAFYERA™ may affect your judgment, thinking, or motor skills.
- Avoid getting too hot or dehydrated.
  - Do not exercise too much.
  - In hot weather, stay inside in a cool place if possible.
  - Stay out of the sun.
  - Do not wear too much clothing or heavy clothing.
  - Drink plenty of water.

**What are the possible side effects of INVEGA HAFYERA™?**

**INVEGA HAFYERA™ may cause serious side effects, including:**

- See **"What is the most important information I should know about INVEGA HAFYERA™?"**
- **Cerebrovascular problems (including stroke) in elderly people with dementia-related psychosis that can lead to death.**
- **Neuroleptic Malignant Syndrome (NMS), a serious condition that can lead to death.** Call your healthcare provider or go to your nearest hospital emergency room right away if you have some or all of the following signs and symptoms of NMS:

- high fever
- confusion
- changes in your breathing, pulse, heart rate, and blood pressure
- stiff muscles
- sweating

- **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
  - feeling as if your heart is pounding or missing beats
- **Uncontrolled body movements (tardive dyskinesia).** INVEGA HAFYERA™ may cause movements that you cannot control in your face, tongue, or other body parts. Tardive dyskinesia may not go away, even if you stop receiving INVEGA HAFYERA™. Tardive dyskinesia may also start after you stop receiving INVEGA HAFYERA™.
- **Problems with your metabolism such as:**
  - **high blood sugar (hyperglycemia) and diabetes.** Increases in blood sugar can happen in some people who receive INVEGA HAFYERA™. Extremely high blood sugar can lead to coma or death. Your healthcare provider should check your blood sugar before you start and regularly during treatment with INVEGA HAFYERA™.

    **Call your healthcare provider if you have any of these symptoms of high blood sugar during treatment with INVEGA HAFYERA™:**

    - feel very thirsty
    - need to urinate more than usual
    - feel very hungry
    - feel weak or tired
    - feel sick to your stomach
    - feel confused, or your breath smells fruity
  - **increased fat levels (cholesterol and triglycerides) in your blood.** Your healthcare provider should check the fat levels in your blood before you start and regularly during treatment with INVEGA HAFYERA™.
  - **weight gain.** You and your healthcare provider should check your weight before you start and often during treatment with INVEGA HAFYERA™.
- **Decreased blood pressure (orthostatic hypotension) and fainting.** You may feel lightheaded or faint when you rise too quickly from a sitting

or lying position, especially early in treatment or when the dose is changed.

- **Falls.** INVEGA HAFYERA™ may make you sleepy or dizzy, may cause a decrease in your blood pressure when changing position (orthostatic hypotension), and can slow your thinking and motor skills which may lead to falls that can cause fractures or other injuries.
- **Low white blood cell count.** Your healthcare provider may do blood tests during the first few months of treatment with INVEGA HAFYERA™.
- **Increased prolactin levels in your blood (hyperprolactinemia).** INVEGA HAFYERA™ may cause a rise in the blood levels of a hormone called prolactin (hyperprolactinemia) that may cause side effects including missed menstrual periods, a reversible reduction in fertility in females who are able to become pregnant, leakage of milk from the breasts, development of breasts in men, or problems with erection.
- **INVEGA HAFYERA™ can make you sleepy or dizzy, and can slow your thinking and motor skills.** Do not drive, operate heavy machinery, or do other dangerous activities until you know how INVEGA HAFYERA™ affects you.
- **Seizures (convulsions).**
- **Difficulty swallowing** that can cause food or liquid to get into your lungs.
- **Prolonged or painful erection lasting more than 4 hours (priapism).** 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 controlling your body temperature so that you feel too warm.** See, "What should I avoid while receiving INVEGA HAFYERA™?"

**The most common side effects of INVEGA HAFYERA™ include:**

- upper respiratory tract infections
- weight gain
- feeling restlessness or difficulty sitting still
- tremors
- shuffling walk
- injection site reactions
- headache
- slow movements
- stiffness

These are not all the possible side effects of INVEGA HAFYERA™.

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

## General information about INVEGA HAFYERA™

Medicines are sometimes prescribed for purposes other than those listed. You can ask your pharmacist or healthcare provider for information about INVEGA HAFYERA™ that is written for health professionals.

**Please click here to read the full Prescribing Information, including Boxed WARNING, for INVEGA HAFYERA™ and discuss any questions you have with your healthcare professional.**

## About the Clinical Trial

The approval of INVEGA HAFYERA™ is based on the results of a randomized, double-blind, non-inferiority Phase 3 global study that enrolled 702 adults (ages 18-70) living with schizophrenia, designed to demonstrate that injection of INVEGA HAFYERA™ is not less effective than INVEGA TRINZA® in delaying time to first relapse in participants previously stabilized on corresponding doses of INVEGA SUSTENNA® or INVEGA TRINZA®.[1] Data showed non-inferiority of INVEGA HAFYERA™ compared to INVEGA TRINZA® on the primary endpoint of time to first relapse at the end of the 12-month period in both intent-to-treat and per protocol analysis sets.

The study consisted of four treatment phases:

- Screening phase (up to 28 days)
- Transition phase (1 to 4 months), applicable to those adult patients who entered the screening phase before being stabilized on INVEGA SUSTENNA® or INVEGA TRINZA®
- Open-label maintenance phase in which adult patients received 1 dose of INVEGA SUSTENNA® at 156 mg or 234 mg dosage or INVEGA TRINZA® at 546 mg or 819 mg dosage and remained in this phase for 1 or 3 months, accordingly
- Double-blind phase (of 12 months), in which all 702 stabilized adult patients were randomized in a 2:1 ratio to receive INVEGA HAFYERA™ (478 patients) or INVEGA TRINZA® (224 patients).[1] Study evaluations included efficacy, safety, pharmacokinetics, and pharmacodynamics

The study's duration, from screening to double-blind endpoint, varied from approximately 13 months to 19 months depending on treatment arm.[1]

**About Long-Acting Injectables**

Long-acting injectables (LAIs) allow for the slow release of medicine into the bloodstream and have been available and studied for more than 50 years.[9] LAI antipsychotics offer a number of potential advantages compared to oral medication, including not having to remember to take medicine daily, improved patient outcomes, improved patient and physician satisfaction, and lower relapse rates.[10] Based on clinical guidance, the National Council for Mental Wellbeing and the American Psychiatric Association recently updated their guidance and practice guidelines to recommend the use of LAIs for appropriate patients.[3,4,5]

**About Schizophrenia**

Schizophrenia is a chronic and severe brain disorder affecting approximately 20 million people worldwide[11] and an estimated 2.8 million adults in the U.S.[12,13] The disease is characterized by distortions in thinking, perception, emotions, language, sense of self, and behavior.[11] It can also lead to neurological impairment and severe disability.[14]

Antipsychotic medication is recognized as an essential component in the treatment of schizophrenia, and adherence to medication plays a critical role in controlling symptoms and costly relapses.[15]

**About the Janssen Pharmaceutical Companies of Johnson & Johnson**

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing

hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology, and Pulmonary Hypertension.

Learn more at www.janssen.com. Follow us at www.twitter.com/JanssenUS and www.twitter.com/JanssenGlobal. Janssen Research & Development, LLC is part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

**Cautions Concerning Forward-Looking Statements**

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding 6-month paliperidone palmitate. 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., any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns 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 descriptions 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 January 3, 2021, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, 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 nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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