

**PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE
PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986**

The medicine is dispensed with a doctor's prescription only

INVEGA[®] 3 mg,

INVEGA[®] 6 mg,

INVEGA[®] 9 mg

Extended-release Tablets

Invega 3 mg contains paliperidone 3 mg

Invega 6 mg contains paliperidone 6 mg

Invega 9 mg contains paliperidone 9 mg

Inactive and allergenic ingredients in the preparation – see chapter 2 section “Important information about some of the ingredients of the medicine” and chapter 6 – “Further information”.

Read the leaflet carefully in its entirety before using the medicine.

This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed for the treatment of your ailment.

Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

The medicine is used to treat schizophrenia in adults and adolescents aged 12 years and above, and schizoaffective disorder in adults.

Therapeutic group: Antipsychotic medicines

Schizophrenia is a disorder with symptoms characterized by hearing, seeing or sensing things that are not there, false beliefs, unusual suspiciousness, becoming withdrawn, incoherent speech, behavioral and emotional flatness (lack of emotional expression). Patients with schizophrenia may also feel depressed, anxious, guilty, or tense.

Schizoaffective disorder is a mental condition in which patients experience a mix of schizophrenia symptoms (as listed above) in addition to mood disorder symptoms (very elated mood, sadness, feeling nervous, distracted, sleeplessness, talkativeness, loss of interest in everyday activities, sleeping too much or too little, eating too much or too little, and recurrent thoughts of suicide).

The medicine can alleviate the symptoms of the disease and prevent them from recurring.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- you are sensitive (allergic) to the active ingredient paliperidone, to risperidone, or to any of the additional ingredients contained in the medicine (see chapter 6 “Further information”).
- you are breastfeeding.

Special warnings regarding use of the medicine

- Patients with schizoaffective disorder treated with this medicine should be carefully monitored for a possible switch from symptoms of mania to symptoms of depression.

- The use of Invega in elderly patients suffering from dementia has not been investigated. However, elderly patients suffering from dementia who are treated with other antipsychotic medicines similar to Invega may be at increased risk of stroke or death (see section 4 – Side effects).

Before treatment with Invega, tell the doctor if:

- you suffer from Parkinson's disease or dementia.
- you have ever been diagnosed with a condition whose symptoms include high temperature and muscle stiffness (also known as neuroleptic malignant syndrome).

- you have ever experienced abnormal movements of the face or tongue (tardive dyskinesia). You should be aware that these conditions may be caused by this type of medicine.
- you have ever suffered from a low white blood cell count (which may or may not have been caused by other medicines).
- you have diabetes or are at risk of developing diabetes.
- you suffer from heart disease or are receiving treatment for heart disease that may cause low blood pressure.
- you suffer from epilepsy.

- you suffer from a swallowing, stomach or intestinal disorders that impair the ability to swallow or pass food through the intestine by normal bowel movements.
- you suffer from diseases associated with diarrhea.
- you suffer from kidney problems.
- you suffer from liver problems.
- you suffer from a prolonged and/or painful erection.
- you suffer from a problem with body temperature regulation or from a rise in body temperature.
- you suffer from abnormally high blood levels of the hormone prolactin or if you may have a prolactin-dependent tumor.

- you or someone else in your family suffers or have suffered in the past from blood clots, as antipsychotics may affect the formation of blood clots.

If you suffer from any of the conditions described above, speak to the doctor. The doctor may want to adjust the dosage of the medicine or monitor you for a while.

Dangerously low levels of certain white blood cells, needed to protect against infections, have been observed on very rare occasions in patients having taken Invega. The doctor may check your white blood cell counts.

Invega may cause weight gain. Significant weight gain may adversely affect your health. Therefore, the doctor must routinely monitor your weight.

Diabetes or worsening of pre-existing diabetes have been observed in patients taking Invega and the doctor should therefore check for signs of high blood sugar levels. In patients suffering from diabetes, blood sugar level monitoring must be performed regularly.

During an operation on the eye for cloudiness of the lens (cataract), the pupil (the black circle in the middle of the eye) may not increase to the desired size. Also, it is possible that the iris (the colored part of the eye) may become floppy during surgery which may lead to eye damage. If you are planning to undergo eye surgery, inform your eye doctor that you are taking this medicine.

Children and adolescents

Treatment of schizophrenia – The medicine is not intended for children under 12 years of age.

Treatment of schizoaffective disorder – The medicine is not intended for children under 18 years of age.

This is because it is not known if Invega is safe and effective in these age groups.

Drug interactions

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

- Problems with electrical conduction in the heart may appear when taking Invega together with certain medicines for treatment of heart rhythm disorders, or other types of medicines, such as antihistamines, antimalarials, or other antipsychotics.

- Since Invega acts primarily in the brain, there is a possibility of interaction with other medicines (or alcohol) that act on the brain because of their additive effect.
- Since the medicine can lower blood pressure, exercise caution when taking it concomitantly with other medicines that lower blood pressure.
- Invega may reduce the effect of medicines for treatment of Parkinson's and restless leg syndrome (e.g., levodopa).
- The effect of Invega may change if you are taking additional medicines that affect the speed of bowel movement (e.g., metoclopramide).

- Reduction of the Invega dosage should be considered when administered concomitantly with valproate.
- It is not recommended taking oral risperidone concomitantly with Invega treatment as the combination may lead to increased side effects.
- Be cautious with concomitant use of Invega with medicines that stimulate the activity of the central nervous system (psychostimulants, such as methylphenidate).

Use of the medicine and alcohol consumption

Avoid alcohol consumption during treatment with Invega.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or are planning to become pregnant, ask your doctor or pharmacist for advice before taking this medicine. Do not take Invega during pregnancy, unless instructed by the doctor.

The following symptoms may occur in newborn babies of mothers that have used Invega in the last trimester of their pregnancy: shaking, muscle stiffness and/or weakness, sleepiness, agitation, breathing problems, and feeding difficulties. If your baby develops any of these symptoms, contact the doctor.

Do not breastfeed during treatment with Invega.

Driving and operating machinery

Use of this medicine may cause dizziness and vision disturbances (see section 4 – Side effects). This should be taken into account in cases where full alertness is required, such as when driving a car or operating machinery.

Important information about some of the ingredients of the medicine

Invega contains lactose

The 3 mg Invega tablet contains lactose (a type of sugar). If you have been told by the doctor that you have an intolerance to certain sugars, consult the doctor before taking the medicine.

Invega contains sodium

This medicine contains less than 1 mmol (23 mg) sodium per tablet, that is, it is considered essentially to be “sodium-free”.

3. HOW SHOULD THE MEDICINE BE USED?

Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen. The dosage and treatment regimen will be determined by the doctor only.

Use in adults

The recommended dose is generally 6 mg once a day, taken in the morning. The dose may be increased or decreased by your doctor within the range of 3 mg to 12 mg once a day for the treatment of schizophrenia or 6 mg to 12 mg once a day for the treatment of schizoaffective disorder. This depends on the effect the medicine has on you.

Use in adolescents

The recommended starting dose for treating schizophrenia in adolescents aged 12 years and above is 3 mg once a day, taken in the morning.

For adolescents weighing 51 kg or more, the dose may be increased within the range of 6 mg to 12 mg once a day.

For adolescents weighing less than 51 kg, the dose may be increased to 6 mg once a day.

The dosage will be determined by your response to the medicine.

Do not exceed the recommended dosage.

Swallow the tablet whole with water or other liquids. Do not chew, break, crush or halve the tablet!

Take the medicine every morning with or without breakfast, but in the same way every day: do not take the medicine with breakfast one day and without breakfast the following day.

The active ingredient, paliperidone, dissolves from the tablet after taking it. The tablet shell is passed out of the body in the stool.

Patients with kidney problems – the doctor may adjust the dosage according to kidney function.

Elderly patients – the doctor may reduce the dosage if kidney function is impaired.

If you took more Invega than you should – contact the doctor immediately. You may experience sleepiness, tiredness, abnormal body movements, difficulty standing and walking, dizziness due to low blood pressure, and heart rhythm disturbances.

If you took an overdose or if a child accidentally swallowed the

medicine, refer immediately to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forgot to take the medicine at the required time, do not take a double dose instead of the forgotten dose. If you missed one dose, take the next dose at the regular time (meaning on the following day) and continue treatment without any change. If you missed two or more doses, contact the doctor.

Adhere to the treatment regimen as recommended by the doctor.

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor or pharmacist.

You should not stop treatment with Invega, since you will lose the effect of the medicine. Do not stop treatment with Invega without an explicit instruction from the doctor as the symptoms may return.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them. If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Invega may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them.

Refer to the doctor immediately if you:

- Experience blood clots in the veins, especially the leg veins (symptoms include: swelling, pain and redness in the legs), which may travel through blood vessels and reach the lungs, causing chest pain and difficulty breathing. If you experience any of these symptoms, immediately seek medical help.
- Suffer from dementia and experience a sudden change in your mental state or you suddenly experience weakness or numbness of the face, arms or legs, especially on one side, or episodes of slurred speech even for a short time. These signs may indicate a stroke.

- Experience fever, muscle stiffness, sweating or decline in the level of consciousness (a disorder called “neuroleptic malignant syndrome”). Immediate medical treatment may be needed.
- Are a man and you are suffering from a prolonged or painful erection (priapism). Immediate medical treatment may be needed.
- Experience involuntary spasms of the tongue, mouth and face. Stopping treatment with Invega may be needed.
- Experience a severe allergic reaction that can be manifested by fever, swelling of the mouth, face, lips or tongue, shortness of breath, itching, skin rash and sometimes a drop in blood pressure (amounting to an anaphylactic reaction).

Very common side effects – effects appear in more than 1 in 10 users:

- Difficulty falling or staying asleep.
- Parkinsonism. This condition may include slow or impaired movement, sensation of stiffness or tightness of the muscles (causing jerky movements), and sometimes even a sensation of movement “freezing up” and then restarting. Other signs include a slow shuffling walk, tremor while at rest, increased salivation and/or drooling, and a loss of expression on the face.
- Restlessness.
- Feeling sleepy or decreased alertness.

- Headache.

Common side effects – effects appear in up to 1 in 10 users:

- Infection in the chest (bronchitis), common cold symptoms, sinus infection, urinary tract infection, flu-like symptoms.
- Weight gain, increased appetite, weight loss, decreased appetite.
- Exaggerated elated mood (mania), irritability, depression, anxiety.
- Dystonia, a condition manifested by slow or sustained involuntary contraction of muscles. While this condition could appear in any part of the body (and may result in abnormal posture), dystonia usually affects the muscles of the face, including abnormal movement of the eyes, mouth, tongue or jaw.

- Dizziness.
- Dyskinesia, a condition manifested by involuntary muscle movements, and can include repetitive, spastic or writhing movements.
- Tremor.
- Blurred vision.
- Impaired electrical conduction between the upper and lower parts of the heart, abnormal electrical conduction in the heart, prolongation of the QT interval, slow heart rate, rapid heart rate.
- Low blood pressure upon standing (consequently, some people taking Invega may experience weakness, dizziness, or may pass out when they stand up or sit up suddenly), high blood pressure.

- Sore throat, cough, stuffy nose.
- Abdominal pain, abdominal discomfort, vomiting, nausea, constipation, diarrhea, indigestion, dry mouth, toothache.
- Elevated liver enzyme levels (transaminases) in the blood.
- Itching, rash.
- Muscle or bone pain, back pain, joint pain.
- Absence of menstrual cycle.
- Fever, weakness, fatigue (tiredness).

Uncommon side effects – effects appear in up to 1 in 100 users:

- Pneumonia, infection of the breathing passages, infection in the bladder, ear infection or tonsillitis.

- A decrease in white blood cell count, decrease in platelets (blood cells that help you stop bleeding), anemia, a decrease in red blood cell count.
- Invega can cause a rise in the level of a hormone called prolactin, detected in a blood test (which may or may not cause symptoms). Symptoms of high prolactin may include: in men – breast swelling, difficulty in getting or maintaining erections, or other sexual dysfunctions. In women – breast discomfort, leakage of milk from the breasts, irregular or other menstrual period problems.
- Diabetes or worsening of diabetes, high blood sugar levels, increased waist circumference, loss of appetite resulting in malnutrition and weight loss, high blood triglyceride level.

- Sleep disorders, confusion, decreased sexual desire, inability to reach orgasm, nervousness, nightmares.
- Tardive dyskinesia (involuntary twitching movements in the face, tongue, or other parts of the body). Tell the doctor immediately if you experience involuntary spastic movements of the tongue, mouth and face. It may be necessary to stop treatment with Invega.
- Convulsions, fainting, an uncontrollable urge to move parts of the body, dizziness upon standing, disturbance in attention, problems with speech, loss of or impaired sense of taste, reduced ability of the skin to feel touch or pain, a sensation of tingling, pricking, or numbness of the skin.

- Oversensitivity of the eyes to light, eye infection, red eyes, dry eyes.
- Spinning sensation (vertigo), ringing in the ears, ear pain.
- Irregular heart rate, abnormal electrical tracing of the heart (ECG), heart pounding (palpitations).
- Low blood pressure.
- Shortness of breath, wheezing, nosebleed.
- Swollen tongue, stomach or intestinal infection, difficulty swallowing, excessive flatulence.
- High blood levels of GGT (a liver enzyme called gamma-glutamyltransferase), high blood levels of liver enzymes.
- Hives (urticaria), hair loss, eczema, acne.

- Elevated blood level of the enzyme CPK (creatine phosphokinase), an enzyme which is sometimes released when there is muscle injury, muscle spasms, joint stiffness, joint swelling, muscle weakness, neck pain.
- Urinary incontinence, frequent passing of urine, inability to pass urine, pain when passing urine.
- Erectile disorders, ejaculation disorders.
- Absence of menstrual periods or other menstrual problems (in women), leakage of milk from the breasts, sexual dysfunction, breast pain, breast discomfort.
- Swelling of the face, mouth, eyes or lips, swelling of the body, arms or legs.

- Chills, an increase in body temperature.
- A change in the way you walk.
- Feeling thirsty.
- Chest pain, chest discomfort, feeling generally unwell.
- Falling.

Rare side effects – (effects appear in up to 1 in 1,000 users):

- Eye inflammation, fungal infection of the nails, infection of the skin, skin inflammation caused by mites.
- Dangerously low level of a certain type of white blood cells, whose function is to fight blood infections.

- A decrease in the number of a certain type of white blood cells, whose function is to protect against infection, a rise in blood eosinophils (a certain type of white blood cell).
- A severe allergic reaction characterized by fever, swollen mouth, face, lips or tongue, shortness of breath, itching, skin rash and sometimes a drop in blood pressure, an allergic reaction.
- Sugar in the urine.
- Abnormal secretion of a hormone that controls urine volume.
- Life-threatening complications of uncontrolled diabetes.
- Dangerously excessive intake of water, low blood sugar level, excessive drinking of water, rise in blood cholesterol.

- Sleepwalking.
- Catatonia – lack of movement or response while awake.
- Lack of emotion.
- Neuroleptic malignant syndrome (confusion, reduced or loss of consciousness, high fever and severe muscle stiffness).
- Loss of consciousness, balance problems and coordination problems.
- Blood vessel problems in the brain, coma due to uncontrolled diabetes, unresponsiveness to stimuli, low level of consciousness, shaking of the head.

- Glaucoma (increased pressure within the eye), increased tears, redness of the eyes, problems with eye movement, eye rolling.
- Atrial fibrillation (an abnormal heart rhythm), rapid heart rate upon standing.
- Blood clots in the veins, especially in the legs (symptoms include swelling, pain and redness in the legs), which may travel through blood vessels to the lungs, causing chest pain and difficulty in breathing. **If you experience these symptoms, seek medical assistance immediately.**
- A decrease in oxygen levels in parts of your body (because of decreased blood flow), flushing.
- Breathing disturbances during sleep, fast, shallow breathing.

- Pneumonia caused by inhaling food, congestion of breathing passages, voice disturbances.
- Blockage in the bowels, stool incontinence, very hard stools, lack of bowel muscle movement that causes blockage.
- Yellowing of the skin and the eyes (jaundice).
- Inflammation of the pancreas.
- Serious allergic reaction with swelling that may involve the throat and lead to difficulty breathing.
- Thickening of the skin, dry skin, skin redness, skin discoloration, flaky itchy scalp or skin, dandruff.

- Breakdown of muscle fibers and muscle pain (rhabdomyolysis), abnormal posture.
- Prolonged and painful erection (priapism). It may require surgical intervention.
- Development of breasts in men, enlargement of the glands in the breasts, discharge from the breasts, vaginal discharge.
- A delay in menstruation, breast enlargement.
- Very low body temperature, a decrease in body temperature.
- Symptoms of drug withdrawal.

Side effects of unknown frequency (effects whose frequency has not been determined)

- Lung congestion.
- High levels of insulin in the blood (a hormone responsible for controlling blood sugar levels).

The following side effects have been observed in patients who took risperidone, which is very similar to paliperidone, and therefore, these side effects can also be expected with Invega:

Sleep-related eating disorder, other blood vessel problems in the brain, crackly lung sounds.

Eye problems during cataract surgery may occur. During cataract surgery, a condition called intraoperative floppy iris syndrome (IFIS) could occur if you are taking or have taken Invega. If you need to have cataract surgery, tell your eye doctor if you are taking Invega or have taken it in the past.

Additional side effects in adolescents

Generally, side effects in adolescents are similar to those seen in adults, except that the following side effects were seen more frequently in adolescents:

- Feeling sleepy or less alert.
- Parkinsonism: This condition may include slow or impaired

movement, sensation of stiffness or tightness of the muscles (making movements jerky), and sometimes even a sensation of movement “freezing up” and then restarting. Other signs include: a slow shuffling walk, tremor while at rest, increased salivation and/or drooling, and a loss of expression on the face.

- Weight gain.
- Common cold symptoms.
- Restlessness.
- Tremor.
- Stomach pain.
- Leaking milk from the breasts in girls.

- Breast swelling in boys.
- Acne.
- Problems with speech.
- Stomach or intestinal infection.
- Nosebleed.
- Ear infection.
- High blood level of triglycerides.
- Sensation of spinning (vertigo).

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link “Report Side Effects of Drug Treatment” found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:
<https://sideeffects.health.gov.il>

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine and any other medicine must be kept in a safe place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.

- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.

Storage Conditions:

Do not store above 30°C.

Store in the original package in order to protect from moisture.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:

The tablet core:

Polyethylene oxide 200K

Polyethylene oxide 7000K

Cellulose acetate

Sodium chloride

Povidone (K29-32)

Hydroxyethyl cellulose

Stearic acid

Butyl hydroxytoluene (E321)

Ferric oxide (Yellow) (E172) (3 mg tablet only)

Ferric oxide (Red) (E172)

Polyethylene glycol 3350

Iron oxide (Black) (E172) (9 mg tablet only)

The color overcoat:

Lactose monohydrate (3 mg tablet only)

Hypromellose

Titanium dioxide (E171)

Polyethylene glycol 400 (6, 9 mg tablet only)

Ferric oxide (Yellow) (E172) (6 mg tablet only)

Ferric oxide (Red) (E172) (6, 9 mg tablet only)

Triacetin (3 mg tablet only)

Carnauba wax

Printing ink:

Purified water

Iron oxide (Black)

Isopropyl alcohol

Propylene glycol

Hypromellose

What the medicine looks like and the contents of the package:

Extended-release tablets in the shape of a capsule.

Invega 3 mg: white tablets imprinted with PAL 3.

Invega 6 mg: beige tablets imprinted with PAL 6.

Invega 9 mg: pink tablets imprinted with PAL 9.

The tablets are supplied in blister packs, containing 28, 30, 49, 56 or 98 tablets per box.

Not all pack sizes may be marketed.

Registration Holder and Address: J-C Health Care Ltd., Kibbutz Shefayim 6099000, Israel.

Manufacturer and Address: Janssen Cilag S.P.A., Via C. Janssen 04100, Borgo S. Michele, Latina, Italy.

Revised in May 2022 according to MOH guidelines.

Registration numbers of the medicine in the National Drug Registry of the Ministry of Health:

Invega 3 mg: 1391531639

Invega 6 mg: 1391631640

Invega 9 mg: 1391731641

INVE ERT PL SH 210622