**Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986**

This medicine is dispensed with a doctor's prescription only

# Perphenan 4 mg
**film-coated tablets**

Name and quantity of active ingredient:
Each tablet contains:
4 mg perphenazine

# Perphenan 8 mg
**film-coated tablets**

Name and quantity of active ingredient:
Each tablet contains:
8 mg perphenazine

For a list of inactive ingredients and allergens, see under 'Important information about some of this medicine's ingredients', and section 6 'Additional information'.

**Read the entire leaflet carefully before you start using this medicine.** This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.
This medicine has been prescribed to treat you. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar to yours.

**Increased mortality in elderly patients with dementia-related psychosis. Elderly patients with dementia-related psychosis treated with antipsychotic medicines are at an increased risk of death. Perphenan is not approved for the treatment of patients with dementia-related psychosis (see SPECIAL WARNINGS).**

## 1. What is this medicine intended for?

- tranquilizer
- prevents vomiting (antiemetic)

**Therapeutic group:** phenothiazine derivative, antipsychotic

## 2. Before using this medicine

**Do not use this medicine:**

- if you are sensitive (allergic) to the active ingredient (perphenazine) or similar compounds, or to any of the other ingredients in this medicine (see section 6).
- in a state of coma or stupor.
- if you are receiving large doses of central nervous system depressants (barbiturates, alcohol, narcotic medicines, analgesics, or antihistamines).
- if you have any blood problems, bone marrow depression, or liver damage.
- if you have established or suspected subcortical brain damage, with or without hypothalamic damage.
- if you have dementia-related psychosis.

**Special warnings about using this medicine:**

- **Increased mortality in elderly patients with dementia-related psychosis**. Elderly patients with dementia-related psychosis who are treated with antipsychotic medicines are at an increased risk of death. Perphenan is not approved for the treatment of patients with dementia-related psychosis.
- **Tardive dyskinesia**. A syndrome consisting of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic

medicines. Older patients are at increased risk of developing tardive dyskinesia. Tell the doctor if signs and symptoms of tardive dyskinesia appear in patients receiving antipsychotic medicines. The doctor will consider stopping the medicine.

- **Neuroleptic Malignant Syndrome**. This potentially fatal syndrome has been reported in association with antipsychotic medicines. The clinical signs are high fever, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or abnormal blood pressure, fast heart rate, excessive sweating, and irregular heart rate).
- **Leucopenia (low number of white blood cells), neutropenia (low number of neutrophils, a type of white blood cell) and agranulocytosis (severe neutrophil deficiency)**. These types of events could be connected to treatment with antipsychotic medicines.
- **Sensitivity to light**. Avoid unnecessary exposure to the sun during Perphenan treatment because this medicine can cause sensitivity to light.
- **Falls**. Perphenan may cause drowsiness, low blood pressure when standing up, motor and sensory instability, which may lead to falls and, consequently, fractures and other injuries. There is an increased risk of hip-joint fracture in the elderly. Elderly patients, must be assessed for this risk, started on lower doses, and be monitored closely. Starting treatment on a lower dose also takes into account a higher frequency of reduced liver function, underlying disease, or treatment with other medication.
- **The elderly**. Elderly patients are particularly sensitive to the side effects of antipsychotic medicines, including Perphenan. The elderly must be started on a lower dosage and monitored closely.
- The antiemetic effect of Perphenan may obscure signs of toxicity caused by overdose of other medicines or make it more difficult to diagnose disorders such as brain tumors or intestinal obstruction.

**Before treatment with Perphenan, tell your doctor if:**

- you have a low white blood cell count or if you have ever used medicines that caused you leucopenia/neutropenia.
- you suffer from depression, have seizures, or alcohol withdrawal symptoms.
- you have ever used another phenothiazine medicine and experienced severe side effects.
- you are about to undergo surgery, tell your anesthetist that you are taking Perphenan.
- you have breathing problems due to acute lung infection or if you have chronic respiratory disorders such as severe asthma or emphysema.

Tell your doctor if you experience slight twisting movements of the tongue. These could be an early sign of tardive dyskinesia syndrome and if the medication is stopped at that time the syndrome may not develop.

**Children and adolescents**
This medicine is not intended for children under 14 years old.

**Tests and follow-up**
Blood counts and liver and kidney functions must be checked periodically during the course of treatment with Perphenan.

**Other medicines and Perphenan**
**If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist.** Particularly if you are taking:

- tricyclic antidepressants and selective serotonin reuptake inhibitors such as fluoxetine, sertraline, and paroxetine.
- medicines for reducing blood pressure: beta blockers.
- medicines for heart rhythm disorders.
- anticonvulsants; a higher dose of an anticonvulsant may be needed when used concomitantly.
- central nervous system depressants (barbiturates, alcohol, narcotic medicines, analgesics, or antihistamines). Do not take any of these medicines together with Perphenan without consulting your doctor.
- atropine or medicines that are like atropine or if you expect to be exposed to extreme heat or to pesticides that contain phosphorus - there is a risk of increase in the anticholinergic effect.

**Pregnancy and breastfeeding**
Do not use this medicine if you are pregnant, think you may be pregnant or are planning to have a baby, or if you are breastfeeding, unless your doctor has decided that this treatment is essential and has weighed the expected benefits against the possible risks to mother and child.
The following symptoms can occur in newborns of mothers who used Perphenan in the last trimester of pregnancy (last three months of pregnancy): agitation, hypertonia (high muscle tone), hypotonia (low muscle tone), hyperreflexia, tremor, sleepiness, respiratory distress and feeding disorder. If your baby develops any of these effects, consult your doctor.

**Using this medicine and food**
You can take this medicine with or without food. Do not take this medicine with coffee or tea.

**Using this medicine and alcohol consumption**
Do not drink wine or other alcoholic beverages while taking this medicine because when used together they may have greater sleep-inducing and blood pressure lowering effects. Due to the potentiating effect of alcohol on the effect of the medicine, the risk of suicide and the danger of overdose may be increased in patients who use alcohol excessively.

**Driving and using machines**
Using this medicine can impair the mental and/or physical abilities you need to perform hazardous activities such as driving or operating machines. Do not drive or operate machines when you start using this medicine and until you are sure that you are not getting these side effects. If you are not sure, consult your doctor before you drive or operate machines.

**Important information about some of this medicine's ingredients**
This medicine contains lactose. If a doctor has told you that you have an intolerance to certain sugars, consult your doctor before using this medicine.

## 3. How to use this medicine?

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.
**Only your doctor will determine your dose and how you should take this medicine, according to your age, condition, and response to previous treatment.**

**The recommended dosage is usually:**
Adults: The usual adult dose is 4 mg three times a day. Your dose may need to be adjusted upward or downward according to your response. Do not exceed a total daily dose of 24 mg.
Elderly: Elderly patients must take one quarter and up to one half of the adult dose.
Children: Do not give Perphenan to children under 14 years old.

**Do not exceed the recommended dose.**

- Do not chew, split, or crush the tablets!
- Swallow the medicine with a glass of water.

**If you forget to take this medicine at the required time**, do not take the missed dose. Wait until the next dose is due and then continue as usual. Never take two doses together!

**If you have accidentally taken a higher dose**, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you**.**
The toxic effects of perphenazine are typically mild to moderate with death occurring in cases involving a large overdose. Overdose of perphenazine primarily involves the extrapyramidal mechanism and produces the same side effects described in section 4, but to a more marked degree. It is usually experienced as stupor or coma; children may have convulsive seizures. Signs of arousal may not occur for 48 hours. The primary effects of medical concern are cardiac in origin including fast heart rate (tachycardia), prolongation of the QRS or QTc intervals, atrioventricular block, torsade de pointes, ventricular dysrhythmia, hypotension or cardiac arrest, which indicate serious poisoning. Deaths by deliberate or accidental overdose have occurred with this class of medicines.

Adhere to the treatment as recommended by your doctor.
Even if your health improves, do not stop taking this medicine without consulting your doctor.

**If you stop taking this medicine**
Do not stop taking this medicine without consulting your doctor, particularly if you have been taking high doses for a long period. When you stop this treatment, your doctor will reduce your dosage gradually because if you stop taking the tablets suddenly after taking high doses of this medicine, it may cause stomach inflammation (gastritis), nausea, vomiting, dizziness, and tremor.

**Do not take medicines in the dark! Check the label and dose every time you take medicine. Wear glasses if you need them.**
**If you have any further questions about using this medicine, consult your doctor or pharmacist.**

## 4. Side effects

Like with all medicines, using Perphenan may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

**Effects on the central nervous system:**
Extrapyramidal reactions:
opisthotonus, trismus, twisting of the neck (torticollis), neck tilted backward (retrocollis), aching and numbness of the limbs, motor restlessness, oculogyric crisis,

hyperreflexia, dystonia, including protrusion, discoloration, aching and rounding of the tongue, tonic spasm of the masticatory muscles, tight feeling in the throat, slurred speech, problem with swallowing (dysphagia), involuntary movements due to medication (akathisia), repetitive involuntary movements (dyskinesia), parkinsonism, and disturbed coordination of voluntary movements (ataxia).
Dystonia:
Symptoms of dystonia: prolonged abnormal contractions of groups of muscles - may occur during the first days of treatment in people who are sensitive to this. Dystonic symptoms include: spasm of the neck muscles, sometimes progressing to tightness of the throat, difficulty swallowing, difficulty breathing, and/or protrusion of the tongue.
Persistent tardive dyskinesia:
As with all antipsychotic medicines, tardive dyskinesia may appear in some patients on long-term therapy or may appear after the medicine has been discontinued. Although the risk appears to be greater in elderly patients on high-dose therapy, especially women, it may occur in patients of either sex and in children. The symptoms are persistent and in some patients appear to be irreversible. The syndrome is characterized by rhythmic, involuntary movements of the tongue, face, mouth or jaw (for example, protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Sometimes these may be accompanied by involuntary movements of the limbs.
Other effects on the central nervous system include: cerebral edema; abnormal proteins in the cerebrospinal fluid; convulsive seizures, particularly in patients with EEG abnormalities or a history of such disorders; and headaches.
Neuroleptic malignant syndrome has been reported in patients treated with antipsychotic medicines (see '**Special warnings about using this medicine**').
Drowsiness may occur, particularly during the first or second week, after which it generally disappears. If this effect is troublesome, the dose should be lowered.
Sleep-inducing (hypnotic) effects appear to be minimal, especially in patients who are permitted to remain active.
Negative behavioral effects include paradoxical exacerbation of psychotic symptoms, catatonic-like states, paranoid reactions, lethargy, paradoxical excitement, restlessness, hyperactivity, nocturnal confusion, bizarre dreams, and insomnia.

**Autonomic Effects:**
Dry mouth or salivation, nausea, vomiting, diarrhea, reduced appetite, constipation, complete constipation, paralytic ileus (bowel obstruction) which if severe can cause complications and death, fecal impaction, urinary retention, passing urine frequently or incontinence, bladder paralysis, passing large volumes of urine, stuffy nose, pallor, constriction of the pupil (miosis), widening of the pupil (mydriasis), blurred vision, glaucoma, sweating, hypertension, hypotension, and occasional change in pulse rate may occur. Significant autonomic effects have been infrequent in patients receiving less than 24 mg perphenazine daily.

**Allergic effects:**
hives (urticaria), redness of the skin (erythema), eczema, skin inflammation with peeling of the skin, itchiness, sensitivity to light, asthma, fever, anaphylactoid reactions, swelling in the throat, and angioneurotic edema; contact dermatitis in nursing personnel administering the medicine; and in extremely rare instances, individual idiosyncrasy or hypersensitivity to phenothiazines has resulted in brain edema, circulatory collapse, and death.

**Endocrine Effects:**
Milk production in women which is unrelated to delivery or breastfeeding, milky breast discharge (galactorrhea), moderate breast enlargement in women and

enlarged breasts in men (gynecomastia) being treated with large doses, disturbances in the menstrual cycle, amenorrhea, changes in libido, inhibition of ejaculation, syndrome of inappropriate ADH (antidiuretic hormone) secretion, false positive pregnancy tests, hyperglycemia, hypoglycemia, sugar in the urine.

**Effects on heart and blood vessels:**
postural hypotension (drop in blood pressure when getting up from lying or sitting down), fast heartbeat (tachycardia) (especially with sudden, sharp increase in dosage), slow heartbeat (bradycardia), cardiac arrest, faintness, and dizziness. Occasionally the hypotension effect may produce a shock-like condition. ECG changes, nonspecific (similar to quinidine effects) and usually reversible, have been observed in some patients receiving phenothiazine antipsychotic medicines. Sudden death has occasionally been reported in patients who have received phenothiazines. In some cases, the death was apparently due to cardiac arrest; in others, the cause appeared to be choking due to failure of the cough reflex. In some patients, the cause could not be determined nor could it be established that the death was due to the phenothiazine medicine.

**Hematological effects:**
Agranulocytosis, eosinophilia, leukopenia, hemolytic anemia, thrombocytopenic purpura, and pancytopenia. Most cases of agranulocytosis occurred between the fourth and tenth weeks of therapy. Patients should be watched closely, especially during that period, for the sudden appearance of sore throat or signs of infection. If white blood cell and differential cell counts show significant cellular depression, stop the medicine and start appropriate therapy. However, a slightly lowered white blood cell count is not in itself an indication to stop the medicine.

**Other effects:**
Special considerations in long-term therapy include pigmentation of the skin, which occurs chiefly in the exposed areas; changes in the eyes consisting of deposition of fine particulate matter in the cornea and lens of the eye, progressing in more severe cases to star-shaped cloudiness in the lens; epithelial keratopathies; and pigmentary retinopathy. Also noted: peripheral edema, reversed epinephrine effect, increase in PBI not attributable to an increase in thyroxine, salivary gland (parotid) swelling (rare), very high fever (hyperpyrexia), systemic lupus erythematosus-like syndrome, increases in appetite and weight, overeating (polyphagia), intolerance of light (photophobia), and muscle weakness.
**In case of unexplained high fever, stop using this medicine.**
Liver damage (biliary stasis) may occur. Jaundice may occur, usually between the second and fourth weeks of treatment, and is regarded as a hypersensitivity reaction. Incidence is low. The clinical picture resembles infectious liver inflammation (hepatitis) but with laboratory features of obstructive jaundice. It is usually reversible; however, chronic jaundice has been reported.

**If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.**

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: **https://sideeffects.health.gov.il**

## 5. How to store the medicine?

- Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.
- **Storage conditions:** Store in a cool and dry place below 25°C.
- Do not throw away medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

## 6. Additional information

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

Perphenan 4 mg:
lactose monohydrate, corn starch, microcrystalline cellulose, gelatin and magnesium stearate.
Coating:
polyvinyl alcohol-partially hydrolyzed, titanium dioxide, PEG 3350 and talc.

Perphenan 8 mg:
lactose monohydrate, corn starch, microcrystalline cellulose, gelatin, sodium starch glycolate and magnesium stearate.
Coating:
hypromellose, titanium dioxide, polydextrose, PEG and black iron oxide.

**What the medicine looks like and contents of the pack:**

Perphenan 4 mg: round, biconvex, white, plain on both sides, film-coated tablet.
The tablets are packaged in a tray (blister). Each package contains 30, 60, or 1,000 tablets.

Perphenan 8 mg: round, biconvex, gray, plain on both sides, film-coated tablet.
The tablets are packaged in a tray (blister). Each package contains 20, 30, or 1,000 tablets.

Not all pack sizes may be marketed.

**Manufacturer and registration holder:** Taro Pharmaceutical Industries Ltd., 14 Hakitor St., P.O.B 10347, Haifa Bay 2624761

**Registration number of the medicine in the Ministry of Health's National Drug Registry:**

Perphenan 4 mg: 015 38 24729 00
Perphenan 8 mg: 123 49 24730 00

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