PATIENT PACKAGE LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

Ridazin 10 mg

Film-Coated Tablets

The active ingredient and its quantity: Each tablet contains:
Thioridazine HCl 10 mg

Ridazin 25 mg

Film-Coated Tablets

The active ingredient and its quantity: Each tablet contains:
Thioridazine HCl 25 mg

Ridazin 100 mg

Film-Coated Tablets

The active ingredient and its quantity: Each tablet contains:
Thioridazine HCl 100 mg

For the list of inactive ingredients, please see section 6.

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 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.
This medicine is not usually recommended for children and infants under 2 years of age.

1. WHAT IS THIS MEDICINE INTENDED FOR?

For treatment of schizophrenic patients who fail to respond adequately to other antipsychotic medicines.

Therapeutic group: The phenothiazines group

2. BEFORE USING THE MEDICINE:

Do not use this medicine:
- if you are sensitive (allergic) to the active ingredient (thioridazine) or any of the other ingredients of the medicine (see section 6).
- in comatose states or in conditions of severe central nervous system depression, including drug induced central nervous system depression (see section "If you are taking, or have recently taken, other medicines").
- if you suffer from serious impairment of heart function.
- in combination with other medicines known to prolong the QT interval (e.g., quinolone antibiotics, terfenadine, astemizole, cisapride, droperidol, haloperidol, risperidone).
- in patients with congenital prolonged QT syndrome or in patients with a history of cardiac arrhythmias.
- in patients with a genetic disorder that causes reduced cytochrome P450 2D6 activity (an enzyme that breaks down medicines).
- in combination with medicines that inhibit the activity of cytochrome P450 2D6 (e.g., fluoxetine and paroxetine) and medicines that inhibit metabolism of thioridazine (e.g., fluvoxamine, propranolol and pindolol).

Special warnings regarding use of this medicine:
- Elderly patients with dementia-related psychosis are at increased risk of death.
- If you are due to undergo surgery (including dental), or any procedure involving anesthesia, inform the anesthesiologist that you are taking this medicine.
- Avoid abruptly switching from a lying or sitting position to standing to avoid dizziness and, in extreme cases, fainting.
- Use of this medicine may cause disturbances in the central nervous system, such as: neuroleptic malignant syndrome (NMS) and tardive dyskinesia (see "Side effects" section).
- Thioridazine may prolong the QT interval in a dosage-dependent manner and therefore may cause arrhythmias (of the Torsades de pointes type) and sudden death. The risk of this may increase when this medicine is taken in combination with certain medicines; therefore, inform the doctor that you are taking Ridazin before taking any new medicines.
- Patients who experienced an allergic reaction to one phenothiazine may have a tendency to develop an allergic reaction to other phenothiazines as well.
- If you have low white blood cell levels or if you have suffered in the past from leucopenia/neutropenia after taking medicines – you are at increased risk of developing leucopenia/neutropenia.
- Tolerance to phenothiazines is lower in elderly patients. The most common side effects in these patients are: parkinsonism (Parkinson-like effects) and akathisia (an uncontrolled need to move). In addition, there is increased risk of agranulocytosis and leucopenia (see "Side effects" section) in elderly patients.
- Schizophrenic patients with epilepsy should continue taking the antiepileptic medicine during the course of treatment with Ridazin.
- When taking a higher dosage than recommended, this medicine may cause an eye disease retinitis pigmentosa, characterized by decreased visual acuity, brown-tinted vision and limited night vision.
- Use of this medicine may impair alertness and therefore requires that caution be exercised when driving a car, operating dangerous machinery and when engaging in any activity that requires alertness. Therefore, take this medicine with caution and increase the dosage gradually.
- Women being treated with the medicine tend to suffer more from orthostatic hypotension than men. Avoid treating hypotension with epinephrine, as phenothiazines can increase the effect of epinephrine. When vasoconstrictors are necessary, levarterenol and phenylephrine are the most suitable.
- Thioridazine may increase the effect of agents that suppress the central nervous system (e.g., alcohol, anesthetics, barbiturates, narcotic agents, opiates, other psychoactive medicines, etc.), of atropine and phosphorous-containing pesticides. Severe respiratory depression and respiratory arrest have been reported in patients who received phenothiazine in combination with barbiturates at a high dosage.

If you are taking, or have recently taken, other medicines including nonprescription medicines and nutritional supplements, tell the doctor or pharmacist. Especially if you are taking:
- medicines that inhibit the cytochrome P450 2D6 enzyme (e.g., fluoxetine, paroxetine). Do not take thioridazine together with these medicines.
- medicines such as fluvoxamine, propranolol and pindolol. Do not take thioridazine together with these medicines since their combination may prolong the QT interval and increase the risk of severe and life-threatening arrhythmias (such as Torsades de pointes-type arrhythmias).
- medicines that prolong the QT interval (affecting the ECG) (e.g., quinolone antibiotics, terfenadine, astemizole, cisapride, droperidol, haloperidol, risperidone) – do not take thioridazine together with these medicines.
- adrenaline (epinephrine).
- agents that depress the central nervous system (e.g., alcohol, anesthetics, barbiturates, narcotic agents, opiates, other psychoactive medicines, etc.), atropine and phosphorous-containing pesticides.

Use of the medicine and food:
Take the medicine with a meal.

Use of the medicine and alcohol consumption:
Do not drink wines or alcoholic beverages during the course of treatment with the medicine.

Pregnancy and breastfeeding:
If you are pregnant or breastfeeding, consult a doctor or pharmacist before using medicines.
Infants who were exposed to antipsychotic medicines during the last trimester of pregnancy, are at increased risk of extrapyramidal symptoms and/or withdrawal symptoms after delivery. Agitation, abnormally high muscle tonus, low muscle tonus, tremor, sleepiness, respiratory distress and feeding disorders have been reported.
Ridazin should be used during pregnancy only if the benefit to the mother outweighs the possible risk to the fetus.

Driving and use of machines:
Use of this medicine may impair alertness and cause vision disturbances and therefore requires that caution be exercised when driving a car, operating dangerous machinery and when engaging in any activity that requires alertness. Children should be cautioned against riding bicycles or playing near the road and the like.

Important information regarding some of the ingredients of the medicine:
The preparation contains lactose and may cause undesirable effects in people with lactose intolerance.

3. HOW SHOULD YOU USE THE MEDICINE?

- Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain.

The dosage and treatment regimen will be determined by the doctor only. The usual dosage is generally:
Adults:
The starting dosage is usually 50-100 mg 3 times a day. The doctor can gradually increase the dosage up to a maximum of 800 mg per day, as needed. After achieving control of the symptoms, the doctor will gradually lower the dosage to determine the minimal maintenance dosage. The daily dosage ranges between 200-800 mg divided into 2-4 doses.
Children:
This medicine is not usually recommended for children and infants under 2 years of age.
The recommended starting dosage is 0.5 mg/kg/day in divided doses. The doctor can gradually increase the dosage until obtaining the optimal therapeutic effect or until reaching the maximum dosage of 3 mg/kg/day.
Use the lowest dosage for the shortest period that provides an adequate clinical response. From time to time, the doctor will evaluate the need for further treatment.

Do not exceed the recommended dose.
- Do not chew, halve or crush!
- Do not hold the medicine in your mouth for longer than necessary to swallow it.

Tests and follow up
Before starting and during the course of treatment, it is recommended to perform an ECG test and to check the blood potassium level, especially during the dosage adjustment periods.
Patients who experienced symptoms that may be related to Torsades de pointes-type arrhythmias (e.g., dizziness, palpitations, fainting), may warrant further cardiac evaluation; particularly, a Holter monitor should be considered.
Patients with low white blood cell levels or patients who have suffered in the past from leucopenia/neutropenia after taking medicines – complete blood cell count should be monitored frequently during the first few months of treatment. Stop treatment if a decline in white blood cell level is observed in the absence of other causes for this decline.
Patients with neutropenia should refer to a doctor for immediate treatment upon occurrence of fever or other signs and symptoms of infection.

If you accidentally took a higher dosage, the following symptoms may appear: cardiac arrhythmias, hypotension, shock, ECG changes, slow heart rate, sinus tachycardia (fast but regular heart rate), atrioventricular block (partial or complete obstruction of conduction of the electrical impulse from the atria to the ventricles), ventricular tachycardia, ventricular fibrillation, Torsades de pointes ("twisting of points"), cardiac depression, sedation (drowsiness), extrapyramidal effects, confusion, agitation, hypothermia, hyperthermia, restlessness, seizures, areflexia, coma, dilation of the pupils, narrowing of the pupils, dry skin, dry mouth, nasal congestion, urinary retention, blurred vision, respiratory depression, apnea, pulmonary edema, digestive tract hypomotility, constipation, ileus, oliguria, uremia (excessive quantities of urea in the blood).
If you took an overdose, or if a child accidentally swallowed the medicine, immediately refer to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forgot to take this medicine at the required time, take a dose as soon as you remember, but never take two doses together.
Adhere to the treatment 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.
- 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 this medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS:

As with any medicine, use of Ridazin may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.

Stop using the medicine and refer to a doctor immediately if:
- you are suffering from tardive dyskinesia – a syndrome characterized by involuntary movements involving the tongue, face, mouth, lips and jaws (e.g., protrusion of the tongue, swelling of the cheeks, puckering of the mouth and chewing movements), the trunk and extremities. The syndrome is sometimes irreversible. The frequency is higher in adults, especially in adult women. Risk of the syndrome, including risk that the syndrome will be irreversible, increases with longer treatment duration and higher dosages. Nevertheless, the syndrome can also develop after a short period of treatment with low dosages. The syndrome can occur during the course of treatment, when lowering the dosage or after stopping treatment.
- you are suffering from neuroleptic malignant syndrome (NMS) that may be life-threatening and its symptoms are: dangerous elevation of body temperature, muscle rigidity, changes in mental state and autonomic instability (irregular pulse or blood pressure, fast pulse, increased sweating and arrhythmias).

Refer to a doctor as soon as possible if:
- you are suffering from prolongation of the QT interval or changes in the ECG.
- you are suffering from symptoms that indicate heart rate disturbances, such as: dizziness, palpitations or fainting.
- you are suffering from leucopenia/neutropenia (reduced white blood cell count), agranulocytosis (severe deficiency in neutrophils, a type of white blood cell).

Additional side effects:
- Drowsiness, especially with high dosages given at the beginning of treatment. This effect usually passes with continued treatment or when lowering the dosage. Parkinson's-like syndrome and other extrapyramidal symptoms. Nocturnal confusion, hyperactivity, lethargy, psychotic reactions, restlessness and headache.
- Dry mouth, blurred vision, constipation, nausea, vomiting, diarrhea, nasal congestion and pallor.
- Increased prolactin levels that can be detected in blood tests and can cause, but not necessarily, symptoms such as: galactorrhea (milk-like secretion from the nipples when not breastfeeding), breast enlargement, amenorrhea, delayed ejaculation, peripheral edema and erectile dysfunction.
- Dermatitis (skin inflammation), urticarial eruptions on the skin and sensitivity to light.
- Swelling of the parotid glands located under the ears.
- Priapism (prolonged and painful erection).
- Seizures.
- Decreased blood pressure when getting up from a lying or sitting position.

Side effects with other phenothiazines:
In addition to the effects listed above, the following side effects have been seen upon use of other medicines from the phenothiazines group:
- Autonomic responses: constriction of the pupils, severe constipation, anorexia, paralytic ileus.
- Skin reactions: erythema, exfoliative dermatitis, contact dermatitis.
- Blood disorders: eosinophilia (increased blood eosinophil count), thrombocytopenia (platelet deficiency), anemia (reduced red blood cell count), aplastic anemia and pancytopenia (simultaneous decrease in red blood cells, white blood cells and platelets).
- Allergic reactions: fever, laryngeal edema, angioedema, asthma.
- Hepatic toxicity: jaundice, biliary statis (obstruction of passage of the bile in the liver).
- Cardiovascular effects: hypotension which, rarely, can cause cardiac arrest.
- Extrapyramidal symptoms: akathisia (uncontrolled need to move), agitation, motor restlessness, dystonic reactions (prolonged contraction of muscle groups), trismus (spasm of the jaw muscles that hold the jaws shut tightly), involuntary spasm of the neck, spasm of the muscles that causes backward curving of the head, neck and spine, oculogyric crisis (rare complication of Parkinson's disease, in which the eyes are fixed, usually upward or sideways, for a few minutes or hours), tremor, muscle stiffness, akinesia (reduced ability to move).
- Endocrinic disturbances: menstrual irregularities, altered libido, weight gain, edema. False-positive pregnancy test results have been reported.
- Urinary system disturbances: urinary retention, urinary incontinence.
- High fever, excitement, bizarre dreams, aggravation of psychosis and confusion. A syndrome characterized by progressive pigmentation of skin regions or of the conjunctiva, sometimes accompanied by discoloration of the exposed parts of the white of the eye or cornea. Clouding of the anterior lens and cornea described as irregular or stellate in shape has also been reported. Systemic lupus erythematosus-like syndrome.

If a side effect occurs, if any of the side effects worsen or if you suffer from a side effect not mentioned in this leaflet, consult with the doctor.

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 in order to avoid poisoning. Do not induce vomiting without explicit instruction from the doctor.
- Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.
- Store below 25°C, in a cool and dark place.
- Do not dispose of medicines in the wastewater or waste bin. Ask the pharmacist how to dispose of medicines no longer in use. These measures will help protect the environment.

6. FURTHER INFORMATION:

In addition to the active ingredient, the medicine also contains:
Ridazin 10 mg:
Lactose monohydrate, Corn starch, Microcrystalline cellulose, Hydroxypropylmethyl cellulose, Talc, Magnesium stearate, Titanium dioxide, Polyethylene glycol, D&C yellow #10 lake, Sunset yellow lake, Indigo carmine lake, Brilliant blue lake.
Each tablet contains 41.6 mg lactose
Ridazin 25 mg:
Lactose monohydrate, Microcrystalline cellulose, Pregelatinized starch, Talc, Hydroxypropylmethyl cellulose, Magnesium stearate, Iron oxide yellow, Polyethylene glycol, Iron oxide black, Iron oxide red, Titanium dioxide.
Each tablet contains 86.9 mg lactose
Ridazin 100 mg:
Lactose monohydrate, Pregelatinized starch, Microcrystalline celulose, Talc, Hypromellose, Magnesium stearate, D&C yellow #10 lake, Polyethylene glycol, Titanium dioxide, FD&C Blue #2 lake, Brilliant blue lake.
Each tablet contains 112.1 mg lactose

What the medicine looks like and the contents of the package:
Ridazin 10 mg:
A film-coated, green, round and biconvex tablet.
The tablets are packaged in a tray (blister). Each package contains 40, 100 or 1,000 tablets.
Ridazin 25 mg:
A film-coated, brown, round and biconvex tablet.
The tablets are packaged in a tray (blister). Each package contains 30 or 1,000 tablets.
Ridazin 100 mg:
A film-coated, green, round and biconvex tablet.
The tablets are packaged in a tray (blister). Each package contains 30, 100 or 1,000 tablets.
Not all package sizes may be marketed.

Manufacturer and license holder: Taro Pharmaceutical Industries Ltd., Haifa Bay 2624761.

Registration numbers of the medicine in the National Drug Registry of the Ministry of Health:
Ridazin 10 mg: 015 26 24726
Ridazin 25 mg: 015 09 24727
Ridazin 100 mg: 015 27 24728

This leaflet was checked and approved by the Ministry of Health in November 2014.