Patient package insert according to Pharmacists' Regulations (Preparations) – 1986

This medicine can be sold with a physician's prescription only

Disothiazide® 25, tablets

Each tablet contains hydrochlorothiazide at a dosage of 25 mg.
Inactive ingredients and allergens - refer to section 6 "Additional information" and section 2 "Important information about some of the ingredients of this medicine".

Read this entire leaflet carefully before using this 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 you. Do not pass it on to others. It might harm them, even if you think their medical condition is similar to yours.

This medicine is not to be used in children and adolescents under the age of 18, since there is no experience with its use in this age group.

1.What is this medicine intended for?

Disothiazide is a diuretic, used to lower high blood pressure and to treat oedema.

Therapeutic group: thiazide diuretic.

2. Before using this medicine

Do not use the medicine if:

- You are hypersensitive (allergic) to the active ingredient (hydrochlorothiazide) or to any of the other ingredients the medicine contains (see section 6), other thiazides or other sulphonamides.
- You have severe disturbances in kidney function [renal insufficiency with small quantity of urine (oliguria) or no urine at all (anuria)].
- You have acute inflammation of the kidney (glomerulonephritis).
- You have severe liver function impairment such as liver failure with impaired consciousness (coma and hepatic precoma).
- You suffer from states of potassium deficiency (hypokalaemia).
- You suffer from states of sodium deficiency (hyponatremia).
- You have decreased blood volume (hypovolemia).
- You have high levels of calcium in your blood (hypercalcemia).
- You have high levels of uric acid in your blood that cause symptoms (patients with a history of gout).
- You suffer from gout.
- You are breastfeeding.

Special warnings regarding the use of this medicine

- **Before treatment with Disothiazide, tell the doctor if** you have had skin cancer in the past, or if you develop an unexpected skin lesion during treatment. Hydrochlorothiazide use may increase the risk of developing skin and lip cancer (non-melanoma skin cancer), particularly in long-term use with high doses. Protect your skin from sun exposure and ultraviolet (UV) radiation during treatment with **Disothiazide.**
- **Do not use this medicine without consulting the doctor before commencing treatment** if you suffer or have suffered in the past from:
  - Impaired function of: the respiratory system (e.g., asthma), the heart and/or blood vessels, the liver or kidney/urinary system (in the case of renal failure the preparation is ineffective and can even be harmful).
  - Allergy
  - Diabetes, latent diabetes or diabetes that has not yet manifested itself
  - Lupus
  - Pancreatitis (inflammation of the pancreas)
  - Severe drop in blood pressure
  - Disturbances in blood flow to the brain
- Do not use this medicine without consulting a doctor if you have had sympathectomy, as this condition may enhance the blood pressure-lowering effects of this medicine.
- Tell the doctor if you are pregnant or planning to become pregnant (see section "Pregnancy, breastfeeding and fertility").
- This medicine may cause special sensitivity with sun exposure (and excessive tanning), therefore avoid sun exposure and ensure appropriate protection (long clothing, hat, sunscreens etc.).
- Inform the doctor if you are about to undergo laboratory tests as treatment with this medicine may affect the results.
- During treatment with **Disothiazide**, you must ensure you drink enough fluids.
- Consult the doctor regarding the need for potassium supplement in your diet as a result of taking the medicine (also see section "Use of this medicine and food").
- In case of unnecessary chronic use (abuse) of a diuretic, a pseudo-Bartter's syndrome may occur which causes water retention in the tissues of the body (oedema).
- While using this medicine, routine follow-up check-ups should be performed - see section "Tests and follow-up".
- If you are sensitive to any food or medicine, tell the doctor before taking this medicine.

Tests and follow-up

Use of this medicine may cause changes in the balance of fluids and electrolytes (such as sodium, potassium, chlorine, calcium, magnesium and phosphate). At the beginning of the treatment period and during the course of treatment, routine tests for blood electrolyte balance (mainly potassium, sodium and calcium) and blood pressure should be performed. Testing electrolytes in the blood and urine is particularly important when there are many incidents of vomiting or upon receiving intravenous fluids.
Routine monitoring of creatinine and urea levels, blood lipids (cholesterol and triglycerides), uric acid, and blood sugar levels should be conducted.
Notify the doctor if you are about to undergo laboratory tests as treatment with this medicine may affect the results.

Drug interactions:

Tell the doctor or pharmacist if you are taking, or have recently taken other medicines, including non-prescription drugs and nutritional supplements.
Especially if you are taking:

- Medicines associated with potassium loss and potassium deficiency in the blood (hypokalaemia), such as diuretics (e.g. furosemide), glucocorticoids, the adrenocorticotropic hormone (ACTH), laxatives, carbenoxolone, amphotericin B, penicillin, salicylic acid and its derivatives - concomitant use with **Disothiazide** may increase potassium loss in the blood. It is recommended to monitor potassium levels. These combinations are not recommended.
- Lithium (e.g. Licarbium) - concomitant use with **Disothiazide** increases lithium's harmful effect on the heart and nervous system. Therefore, this combination is not recommended. If the combination is necessary, use only under close medical supervision; monitoring lithium levels is advised.
- Cholesterol lowering medicines such as cholestyramine or colestipol - concomitant use reduces the uptake of **Disothiazide.**
- Salicylates and other non-steroidal anti-inflammatory medicines (NSAIDs) (e.g. indomethacin), including selective COX-2 inhibitors - these medicines may reduce the blood pressure-lowering and diuretic effects of **Disothiazide**. There are isolated cases of worsening of renal function, especially in patients with pre-existing impaired renal function. When salicylates are taken at a high dose, their toxic effect on the central nervous system could be enhanced. In patients who develop hypovolemia (low blood volume) during treatment with **Disothiazide**, concomitant use with NSAIDs may cause severe renal failure.
- Digitalis-based glycosides for cardiac problems (e.g. digoxin) - the effects and side effects of these medicines may be enhanced.
- Steroids
- Insulin or oral anti-diabetic medicines, medicines for treatment of gout (e.g. probenecid, sulfinpyrazone), adrenaline or noradrenaline given, for example, with anaesthetics at the dentist- the effect of these medicines may weaken when given concomitantly with **Disothiazide**. The dosage of these medicines may need to be adjusted.
- Metformin-use with caution due to the risk of hyperacidity of the blood as a result of hydrochlorothiazide-related renal failure.
- Cytostatic medicines (e.g. cyclophosphamide, fluorouracil, methotrexate) - increased bone marrow toxicity may occur, mainly a decrease in specific white blood cells (granulocytopenia).
- The effect of curare-type muscle relaxants such as tubocurarine (administered during certain surgeries) may be increased or prolonged when given concomitantly with **Disothiazide**. Inform the anaesthesiologist that you are being treated with this medicine prior to surgery.
- Methyldopa - cases of breakdown of red blood cells (haemolysis) were reported in concomitant use.
- Preparations affected by serum potassium disturbances. Monitoring of potassium levels and ECG performance is recommended when **Disothiazide** is administered with the following medicines:
  - Antiarrhythmic medicines (e.g.: quinidine, hydroquinidine, disopyramide, amiodarone, sotalol, dofetilide, ibutilide)
  - Certain antipsychotics (e.g.: thioridazine, chlorpromazine, levomepromazine, trifluoperazine, cyamemazine, sulpiride, sultopride, amisulpride, tiapride, pimozide, haloperidol, droperidol)
  - Other medicines (e.g.: bepridil, cisapride, diphemanil, intravenous erythromycin, halofantrine, misolastine, pentamidine, sparfloxacin, terfenadine, intravenous vincamine)
- Allopurinol - use of thiazides may increase the incidences of allergic reaction to allopurinol.
- Amantadine - thiazides may increase the risk of side effects caused by amantadine.
- Calcium salts - thiazide diuretics may increase serum calcium levels. If calcium supplements are needed, calcium levels should be monitored and the calcium dosage adjusted accordingly.
- Vitamin D supplements - concomitant use may increase calcium levels due to decreased calcium excretion from the body.
- Ciclosporin - concomitant use may increase the risk of elevated uric acid levels and gout-like complications.
- Carbamazepine - concomitant use may reduce blood sodium levels. Therefore, blood sodium levels should be monitored.
- Quinidine - the excretion of quinidine may be reduced when used with **Disothiazide.**
- Tetracyclines - concomitant use may cause an increase in serum urea levels.
- Barbiturates, alcohol or narcotic substances - concomitant use may increase the risk and severity of hypotension caused by a change in posture.
- Beta blockers and diazoxide - concomitant use may increase the risk for elevated blood sugar levels (hyperglycaemia).
- Thiazides may increase or accelerate the activity of other blood pressure-lowering medicines, such as ACE inhibitors (e.g.: captopril, enalapril) - there is a risk of an extreme drop in blood pressure at the beginning of treatment and worsening of kidney function. Treatment with diuretics should be discontinued 2-3 days prior to commencing treatment with ACE inhibitors in order to reduce the risk of drop in blood pressure at the beginning of treatment.
- The blood pressure-lowering effect of **Disothiazide** can be increased by concomitant use with other diuretics, blood pressure-lowering medicines, beta blockers, nitrates, barbiturates, phenothiazines, tricyclic antidepressants, vasodilators and alcohol.

Use of this medicine and food

The medicine can be taken with food at breakfast with a sufficient amount of fluids.
During treatment with this medicine, drink sufficient amounts of fluids. Due to increased potassium loss, potassium-rich foods (e.g.: bananas, vegetables, nuts) should be consumed.

Use of this medicine and alcohol consumption

Do not drink alcoholic beverages during treatment with this medicine.

Pregnancy, breastfeeding and fertility

Do not take this medicine during pregnancy. Tell the doctor if you are pregnant, planning to become pregnant or think you are pregnant. Usually, the doctor will recommend that you use a different medicine instead of **Disothiazide**, which is not intended for use during pregnancy. This is because **Disothiazide** penetrates the placenta and using it after the third month of pregnancy may harm the foetus or new-born, such as: risk of jaundice, low platelet count (thrombocytopenia) and other side effects that occur in adults.

If you are breastfeeding, do not take **Disothiazide** as this medicine may inhibit the production of milk. Thiazides are excreted in breast milk and can cause severe side effects in nursing babies, and therefore the doctor must decide whether to discontinue breastfeeding or use of this medicine, depending on its importance to the mother.

Driving and use of machinery

Disothiazide has a mild-moderate effect on the ability to drive and use machinery. Even when used as instructed, this medicine may alter your reactions. Therefore, your ability to drive, operate machinery or work in high altitude in unprotected sites may be impaired. Especially at the beginning of the treatment, when the dose is increased, the preparation is replaced or combined with alcohol.

Important information about some of the ingredients of this medicine

Disothiazide tablets contain lactose**.** If you have been told in the past by a doctor that you are intolerant to certain sugars, consult a doctor before commencing treatment with this medicine.

3. How to use this medicine?

Always use this medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are unsure about the dosage and manner of treatment.

The dosage and manner of treatment will be determined by the doctor only. Generally, the usual dosage is:
High blood pressure: the initial dosage is half a tablet or one tablet per day (12.5-25 mg per day). The long term dosage is usually half a tablet per day (12.5 mg per day).
Cardiac, hepatic or renal oedema: the initial dosage is 25 mg or 50 mg per day.
The long term dosage is usually 25 mg to 100 mg per day.
Patients with impaired kidney, liver or heart function: the dosage should be adjusted.
Elderly patients (over 65 years old): attention should be paid to the possibility of limited renal function.

This medicine is to be taken at regular intervals as determined by the attending doctor.

Do not exceed the recommended dose.

Method of administration:

- Swallow the medicine with water.
- You may halve the tablet. There is no information about crushing or chewing.

If you have accidentally taken a higher dose

If you have taken an overdose or if a child has accidentally swallowed the medicine, proceed immediately to a doctor or to a hospital emergency room and bring the package of the medicine with you.
The symptoms of acute or chronic overdose depend on the amount of fluids and electrolytes lost. When fluid and sodium loss is evident, symptoms may include thirst, feeling of weakness and dizziness, muscle pain and cramps and headaches. Furthermore, rapid heart rate, low blood volume and postural hypotension disorders may occur. The consequence of dehydration and reduced blood volume is thickening of the blood. In addition, convulsions, vague recognition, lethargy, confusion, collapse of the circulatory system, and severe renal failure may occur. Loss of potassium may cause fatigue, muscle weakness, sensory disturbances, paralysis, apathy, flatulence, constipation or arrhythmia. Severe loss of potassium can lead to bowel obstruction or impaired consciousness or loss of consciousness. The most common observed signs and symptoms were those caused by decreased electrolytes (hypokalaemia, hypochloraemia, hyponatremia) and dehydration due to excessive urination. In addition, in the event of concomitant use with digitalis, potassium loss may increase cardiac arrhythmias.

If you forgot to take this medicine

Do not take a double dose in order to compensate for a forgotten dose, treatment should continue as usual. Persist with the treatment as recommended by the doctor.
Refer to the doctor or pharmacist if you feel the effect of the medicine is too strong or too weak.

If you discontinue this medicine

The duration of treatment is unlimited and depends on the type and severity of your illness. After long term use, use should be gradually discontinued.
Even if your health improves, do not discontinue treatment with this medicine without consulting the doctor or pharmacist.

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

4. Side effects

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

Stop the use of this medicine and refer to a doctor if the following side effects appear:

- Allergic skin reaction, the symptoms of which may include itching, reddening of the skin, allergic rash caused by exposure to light, purpura and urticaria, skin irritation or skin rash.
- Yellowing of the skin or eyes.
- Bruises.
- Erythema multiform, including Stevens-Johnson syndrome (diffuse rash with blisters and scaling of the skin mainly around the mouth, nose, eyes and genitals), scaling of the skin over vast areas (exfoliative dermatitis), including toxic epidermal necrolysis.
- Signs of fluid and electrolyte imbalance (mainly a decrease in the levels of potassium, sodium, magnesium, and chloride, and an increase in blood calcium levels); in high dosages, loss of fluids and sodium can occur, usually manifested by dry mouth, thirst, feeling of weakness and dizziness, muscle cramps or muscle pains, headache, nervousness, strong heartbeats (palpitations), regulation disorders of blood pressure related to body position.
- Sleepiness, drowsiness, restlessness, muscle spasms, convulsions, tachycardia (increased heart rate), hypotension, loss of balance due to drop in blood pressure, paraesthesia, small quantity of urine.
- Gastrointestinal disorders such as nausea and vomiting, diarrhoea, abdominal pains and cramps, unusual abdominal pain with nausea and vomiting, sensitivity in bowel functions, anorexia, inflammation of the pancreas, inflammation of the salivary glands.
- Vision problems such as blurred vision, colour vision (yellow-coloured vision) acute temporary near-sightedness, acute narrow-angle glaucoma (symptoms include an acute decrease in vision acuity or in ocular pain).
- Changes in tests: blood tests [e.g.: aplastic anaemia (anaemia due to a disturbance in the production of blood cells in the bone marrow), low white blood cells, reduction in blood platelets (sometimes with purpura), hyperglycaemia, hyperuricemia], excessive glucose in the urine.
- Necrotizing inflammation of the blood vessels.
- Respiratory distress including pneumonia and pulmonary oedema.
- Central nervous system disorders, acute inflammation in the gallbladder, worsened near-sightedness, severe renal failure.

Additional side effects

- Loss of balance when rising from a sitting or lying position (may be aggravated due to consumption of alcohol, barbiturates or narcotic substances), vertigo, increased sensitivity of the skin to sunlight.
- Cases of increased urine excretion leading to dehydration and reduced blood volume may cause the blood to thicken. In more rare cases convulsions, vague recognition, confusion, circulatory system collapse and severe renal failure may occur. In the event of severe renal failure, the doctor will consider whether to suspend or discontinue the treatment.
- Thrombosis and embolism have been reported, especially in elderly patients or patients with venous diseases.
- Loss of potassium may cause fatigue, drowsiness, muscle weakness, paralysis, apathy, constipation and accumulation of gas in the gastrointestinal tract or arrhythmias. Severe loss of potassium may lead to complete or partial bowel obstruction, disturbances of consciousness or loss of consciousness.
- ECG changes and increased sensitivity to preparations containing digitalis (sensitivity to glycoside) may occur. Increased excretion of magnesium in the urine is common, and only occasionally causes magnesium deficiency in the blood.
- Loss of electrolytes and fluids may cause or worsen metabolic alkalosis.
- Raised levels of certain blood liver enzymes; jaundice; occurrence or worsening of systemic lupus erythematosus; gastric irritation; renal dysfunction; baldness.

Very common side effects - (effects that appear in more than 1 out of 10 users): Raised levels of uric acid that may lead to gout attacks in predisposed patients, increased blood lipids (cholesterol and triglycerides), raised blood sugar levels (hyperglycaemia) and increased excretion of sugar into the urine (glycosuria) have been observed in individuals with healthy metabolism, in patients with early stages of diabetes (latent diabetes) or in diabetics, and patients with potassium deficiency.

Common side effects - (effects that appear in 1-10 out of 100 users): Temporary increase in urine-excreted substances (creatinine, urea), loss of appetite, strong heartbeats (palpitations).

Uncommon side effects - (effects that appear in 1-10 out of 1000 users): Anaphylactic reaction, limited tear fluid formation, vascular inflammation, shortness of breath, acute interstitial pneumonia, acute kidney inflammation, impotence, fever caused by an allergic reaction to the medicine.

Rare side effects - (effects that appear in 1-10 out of 10,000 users): Sleep disorders, depression, constipation, dizziness, headaches, sensory disturbances in the limbs.

Very rare side effects - (effects that appear in less than 1 out of 10,000 users):
Bone marrow depression, a major reduction in the number of white blood cells with a tendency toward infections and severe general symptoms (agranulocytosis), haemolytic anaemia, autoimmune haemolytic anaemia, hyperchloremic acidosis, severe skin reactions such as toxic epidermal necrolysis, cutaneous lupus erythematosus, lupus erythematosus-like reaction and recurrence of lupus erythematosus; pulmonary oedema.

Side effects of unknown frequency (effects whose frequency has not yet been determined): Lips and skin cancer (non-melanoma type skin cancer), worsening of the metabolic state in diabetics, onset of latent diabetes, any diabetes that has not yet manifested itself may become worse; in cases of pre-existing gallstones an acute inflammation of the gallbladder may occur.

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

Side effects can be reported to the Ministry of Health via the link "דיווח על תופעת לוואי עקב טיפול תרופתי" that can be found on the home page of the Ministry of Health website (www.health.gov.il) directing to the online form of adverse events reporting or via the following link: https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@mohgov.il

5. How to store this medicine

- Avoid poisoning! This medicine, and all other medicines, must be stored 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 a 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.
- **Storing conditions:** Store at a temperature not exceeding 25°C. Store in the original package.

6.Additional information

In addition to the active ingredient, the medicine also contains:
Lactose monohydrate, maize starch, microcrystalline cellulose, magnesium stearate, carmellose sodium, silica colloidal anhydrous, orange lake (E110).

What the medicine looks like and contents of the package:
Convex light orange tablets with a dividing line on one side. Number of tablets per package: 10, 25, 28, 30, 50, 500, 1000. Not all package sizes may be marketed.

This leaflet was checked and approved by the Ministry of Health in July 2014 and updated in February 2019.

Drug registration number at the national medicines registry of the Ministry of Health: 032 85 21827 00

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