PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986
The medicine is dispensed with a doctor's prescription only

Ripalid 0.5 mg
Ripalid 1 mg
Ripalid 2 mg
Tablets

Each tablet of Ripalid 0.5 mg contains
Repaglinide 0.5 mg
Each tablet of Ripalid 1 mg contains
Repaglinide 1 mg
Each tablet of Ripalid 2 mg contains
Repaglinide 2 mg
Inactive and allergenic ingredients: see section 6 in the leaflet.

Read this leaflet carefully in its entirety 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 to treat your ailment. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar.
This medicine is not intended for adolescents under the age of 18 or for adults over the age of 75.

1. WHAT IS THE MEDICINE INTENDED FOR?

1. Ripalid is intended for the treatment of type 2 diabetes mellitus in adults whose high blood sugar levels are not adequately controlled by diet, weight reduction and exercise.
2. Ripalid is intended for the treatment of type 2 diabetes mellitus, in combination with metformin, in adult patients whose diabetes mellitus is not adequately controlled on metformin alone.

Treatment should be initiated as an adjunct to diet and exercise, to lower the blood glucose levels in relation to meals.
Ripalid is an oral Type 2 antidiabetic medicine, containing repaglinide which helps the pancreas produce more insulin and thereby lowers the blood sugar (glucose) level. **Type 2 diabetes** is a disease in which the pancreas does not secrete enough insulin to regulate the blood sugar level or when the body does not respond normally to the insulin it produces.
Ripalid has shown efficacy in lowering the blood sugar levels, which helps prevent complications from your diabetes.

Therapeutic group: medicines for the treatment of diabetes from the meglitinide group.

2. BEFORE USING THE MEDICINE

Do not use Ripalid if:
- you are sensitive (allergic) to the active ingredient repaglinide or to any of the additional ingredients contained in the medicine (see section 6 in this leaflet).
- your diabetes is type 1 diabetes (insulin-dependent diabetes).
- you have raised acid levels in the blood (diabetic ketoacidosis).
- you have a severe liver disease.
- you are being treated with gemfibrozil (a medicine used to lower high blood fat levels).

Special warnings regarding use of the medicine
Before treatment with Ripalid, tell the doctor:
- If you have liver function problems. Ripalid is not recommended in patients with moderate liver disease. Ripalid should not be used in the case of severe liver disease.
- If you have kidney function problems. Ripalid should be taken with caution.
- If you are about to have major surgery or you have recently suffered from a severe illness or infection. In such cases diabetic control may be lost.
- If you are under the age of 18 or over the age of 75, treatment with Ripalid is not recommended. There have been no studies conducted regarding treatment with the medicine in these age groups.

Tell the doctor if any of the conditions apply to you. Treatment with Ripalid may not be suitable for you. The doctor will instruct you what to do.

Children and adolescents
Do not take this medicine if you are under 18 years of age.

If you experience hypoglycemia (low blood sugar level):
You may experience 'hypo' (short for hypoglycemia: low blood sugar level) which may occur in the following cases:
- If you take too much Ripalid
- If you exercise more than usual
- If you take additional medicines or if you suffer from liver or kidney problems (see "Drug interactions" section below).

Warning signs of hypoglycemia, which may come on suddenly, and can include: cold sweat, cold pale skin, headaches, rapid heartbeat, nausea, a sensation of extreme hunger, temporary changes in vision, drowsiness, unusual tiredness and weakness, nervousness or tremor, anxiety, confusion, concentration difficulties.
If your blood sugar level is low or if you feel a hypoglycemic event coming on, eat a glucose (sugar) tablet or a lot of any sugar-rich food or beverage, and then rest.
When signs of hypoglycemia have disappeared or when blood sugar levels are controlled, continue Ripalid treatment.
You should tell people that are close to you that you have diabetes and that if you pass out (lose consciousness) due to hypoglycemia, you should be laid on your side, and immediately get medical assistance. You should not be given any food or drink if you are unconscious in order to prevent choking.
- If severe hypoglycemia is not treated, it may cause brain damage (temporary or permanent) and even death.
- If you suffer from hypoglycemia that makes you pass out, or from many incidents of hypoglycemia, talk to your doctor. It may be necessary to change the dosage of Ripalid, or make a change in diet or exercise.

If the sugar level in your blood rises:
The blood sugar level may get too high (hyperglycemia). Hyperglycemia can be caused:
- If you take too low a dose of Ripalid.
- If you have an infection or a fever.
- If you eat more than usual.
- If you exercise less than usual.

The warning signs of hyperglycemia appear gradually and include: increased urination, thirst, dry skin and dry mouth. Talk to your doctor. It may be necessary to change the dosage of Ripalid, or to make a change in diet or exercise.

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

Other medicines and Ripalid
You can take Ripalid together with metformin, another medicine for treating diabetes, if the doctor prescribes it for you.
If you take gemfibrozil (a medicine to lower high blood fat levels), you should not take Ripalid.

Your body's response to treatment with Ripalid may change if you use other medicines, such as:
- Medicine from the monoamine oxidase inhibitors (MAOI) group (used to treat depression)
- Beta blockers (used to treat certain heart conditions and hypertension)
- ACE-inhibitors (used to treat certain heart conditions)
- Salicylates (e.g., aspirin)
- Octreotide (used to treat cancer)
- Nonsteroidal anti-inflammatory drugs (NSAIDs, a type of painkillers)
- Steroids, anabolic steroids and corticosteroids (to treat anemia or inflammation)
- Oral contraceptives
- Diuretics (thiazides)
- Danazol (used to treat breast cysts or endometriosis)
- Preparations for the thyroid gland (to treat low levels of thyroid gland hormones)
- Sympathomimetics (to treat asthma)
- Clarithromycin, trimethoprim, rifampicin (antibiotic medicines)
- Itraconazole, ketoconazole (antifungal medicines)
- Ciclosporin (to suppress the immune system)
- Deferasirox (to treat chronic iron overload)
- Clopidogrel (to prevent blood clots)
- Phenytoin, carbamazepine, phenobarbital (to treat epilepsy)
- *Hypericum* (St. John's wort) (a medicinal herb, to treat depression)

Use of Ripalid and food
Take Ripalid before the main meals.

Use of Ripalid and alcohol consumption
Alcohol can change the ability of Ripalid to reduce the blood sugar levels. Pay attention to signs of a hypoglycemia mentioned above.

Pregnancy and breastfeeding
If you are pregnant, breastfeeding or think you are pregnant or plan to become pregnant, consult with your doctor before taking the medicine. Do not take Ripalid if you are pregnant or plan to become pregnant. Do not take Ripalid if you are breastfeeding.

Driving and operating machinery
Your ability to drive or operate machinery may be affected if your blood sugar level is low or high. Bear in mind that you could endanger yourself or other people. You should consult with your doctor whether you can drive a car in the following cases:
- If you suffer from frequent hypoglycemia incidents.
- If your warning signs of hypoglycemia are reduced or non-existent.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the medicine. The dosage and treatment regimen will be determined by the doctor only.
- **The usual starting dosage is generally** 0.5 mg before each main meal. Take the tablets with a glass of water immediately before or up to 30 minutes before each main meal.
- The tablet should be swallowed whole. There is no information regarding halving or crushing the tablet.
- The dosage will be adjusted by your doctor, up to a dosage of 4 mg, to be taken with a glass of water immediately before or up to 30 minutes before each main meal. The maximum recommended daily dose is 16 mg.

Do not exceed the recommended dose.
Do not take more tablets than the doctor has recommended for you.

If you accidentally take a higher dosage
If you take too many tablets, your blood sugar level may become too low, leading to hypoglycemia. See section 2 "If you experience hypoglycemia" for an explanation of this condition and how to treat it.
If you took an overdose, or if a child has 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 forget to take the medicine
If you forget to take this medicine at the designated time, do not take a double dose. Take the next dose at the usual time and consult the doctor. 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.

If you stop taking the medicine
You should know that the desired effect is not achieved and the condition of your diabetes may get worse. If any change in the treatment is necessary, consult the doctor first.

Do not take medicines in the dark! Check the label and the dose <u>each time</u> you take a 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 Ripalid may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

<u>Hypoglycemia</u>
The most frequent side effect is hypoglycemia which may affect up to 1 in 10 users (see in section 2 "If you experience a hypoglycemia"). Hypoglycemic reactions are generally mild to moderate, but may occasionally develop into hypoglycemic unconsciousness or coma. In this case, get medical assistance immediately!

<u>Allergy</u>
Allergy is very rare (may affect up to 1 in 10,000 users). Signs such as swelling, breathing difficulties, rapid heartbeat, dizziness and sweating – all these could be signs of an anaphylactic reaction. Contact a doctor immediately!

Other side effects
Common side effects (occur in 1-10 in 100 users):
- Abdominal pain
- Diarrhea

Rare side effects (occur in 1-10 in 10,000 users):
Acute coronary heart disease (not necessarily due to the medicine)

Very rare side effects (occur in less than one in 10,000 users):
- Vomiting
- Constipation
- Blurry vision
- Severe liver problems
- Abnormal liver function
- Increased liver enzymes in the blood

Side effects of unknown frequency (effects whose frequency has not yet been determined)
- Hypersensitivity (such as rash, itchy skin, reddening of the skin, swelling of the skin)
- Nausea

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

<u>Reporting side effects</u>:
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 following link:
https://sideeffects.health.gov.il
Additionally, you can report to Padagis via the following address: padagis.co.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 carton package and blister package. The expiry date refers to the last day of that month.

Storage conditions
Store in the original package below 25°C.
Do not discard medicines via wastewater or household waste. Ask the pharmacist how to discard medicines you no longer need. Taking these measures will help protect the environment.

6. ADDITIONAL INFORMATION

- In addition to the active ingredient, the medicine also contains the following inactive ingredients: Microcrystalline cellulose, Maize starch, Calcium hydrogen phosphate anhydrous, Polacrilin potassium, Meglumine, Poloxamer, Magnesium stearate, Povidone, Glicerolo anhydrous
  Ripalid 1 mg also contains Yellow iron oxide
  Ripalid 2 mg also contains Red iron oxide

<u>What the medicine looks like and the contents of the package</u>
- Ripalid 0.5 mg tablet is round and colored white.
- Ripalid 1 mg tablet is round and colored yellow.
- Ripalid 2 mg tablet is round and colored red.

The tablets are packaged in trays (blisters) in packs of 30, 90 or 120 tablets. Not all pack sizes may be marketed.
- **Registration holder and address:** Padagis Israel Agencies Ltd., 1 Rakefet St., Shoham.
- Revised in March 2023 according to MOH guidelines.
- Registration numbers of the medicine in the National Drug Registry of the Ministry of Health:
  Ripalid 0.5 mg: 159-05-34990
  Ripalid 1 mg: 158-17-33936
  Ripalid 2 mg: 158-18-33935