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

This medicine is marketed upon physician's prescription only

RIZALT® 10 mg Tablets

RIZALT RPD® 10 mg Wafers

Each tablet contains:	Each RPD wafer contains:
Rizatriptan 10 mg (as benzoate)	Rizatriptan 10 mg (as benzoate)

For a list of inactive ingredients refer to section 6. See also section 2.7 “Important information about some of the ingredients of **RIZALT** Tablets and **RIZALT RPD** Wafers”.

Unless otherwise stated, the information in this Patient Information Leaflet applies to both **RIZALT** Tablets and **RIZALT RPD** Wafers.

Read the entire leaflet carefully before using this medicine.

- This leaflet contains concise information about **RIZALT** Tablets and **RIZALT RPD** Wafers**.** If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. 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 intended for adults above 18 years of age.

1. WHAT RIZALT IS INTENDED FOR?

RIZALT is used for the acute treatment of migraine attacks in adults, with or without aura.

RIZALT is not to be used to prevent migraine attacks.
RIZALT is not for the treatment of hemiplegic or basilar migraines.
It is not known if **RIZALT** is safe and effective for the treatment of cluster headaches.

THERAPEUTIC GROUP: RIZALT belongs to a class of medicines called selective 5-$HT_{1B/1D}$ receptor agonists or Triptans.

2. BEFORE USING RIZALT

2.1 Do not use RIZALT if:

- you are allergic (hypersensitive) to rizatriptan benzoate or any of the other ingredients of **RIZALT** (for the list of inactive ingredients see section 6).
- you have or have had heart problems.
- you have or have had a stroke or a transient ischemic attack (TIA).
- you have or have had blood vessel problems including ischemic bowel disease.
- you have uncontrolled high blood pressure.
- you are concurrently taking antidepressant drugs from the monoamine oxidase (MAO) inhibitors group or have taken a MAO inhibitor within the last two weeks (see also section 2.3 "Interactions with other medicines”).

- you have taken any other drug in the same class (Triptans), such as sumatriptan, naratriptan, zolmitriptan, eletriptan, to treat your migraine in the last 24 hours (see also section 2.3 "Interactions with other medicines").
- You have taken ergotamine containing medicines such as ergotamine, dihydroergotamine, or methysergide in the last 24 hours (see also section 2.3 "Interactions with other medicines").
- you have hemiplegic or basilar migraines.

Talk to your doctor before taking this medicine if you have any of the conditions listed above or if you are not sure if you take any of these medicines.

2.2 Special warnings regarding use of RIZALT

Before starting treatment with RIZALT, tell your doctor if:

- you have or have had heart problems (such as heart attack, decreased blood flow to the heart, or changes in the rhythm or rate of the heartbeat), high blood pressure, chest pain, or shortness of breath.
- you have any risk factors for heart disease or blood vessel disease such as high blood pressure, diabetes, high cholesterol, obesity, smoking, family history of heart problems, you are a post-menopausal woman, you are a male over 40.
- you have or have had any allergies.
- you have phenylketonuria (PKU). **RIZALT RPD** Wafers contain phenylalanine (see also section 2.7 "Important information about some of the ingredients of **RIZALT** Tablets and **RIZALT RPD** Wafers").
- you are pregnant or plan to become pregnant, or if you are breastfeeding, or plan to breastfeed (see section 2.5 "Pregnancy and breast-feeding").
- you are taking or plan to take any drugs, including those obtained without a prescription, and those you normally take for a migraine (see section 2.3 "Interactions with other medicines") because an exacerbation of headache (MOH – medication overuse headache) can develop due to overuse of medicines for the treatment of migraine (such as: ergotamine, triptans, opioids or using a combination of these medicines for more than 10 days in one month).
- If you take **RIZALT** too often, this may result in you getting chronic headaches. In such cases, you should contact your doctor, as you may have to stop taking **RIZALT**.
- you are suffering or have suffered in the past from kidney or liver problems.
- you have any other medical condition.
- Tell your doctor about your symptoms. Your doctor will decide if you have migraine. You should take **RIZALT** only for a migraine attack. **RIZALT** should not be used to treat headaches that might be caused by other, more serious neurological conditions.

2.3 Interactions with other medicines

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

Medicines that should not be taken concomitantly with RIZALT (see section 2.1 "Do not use **RIZALT** if:"):

- Do not take **RIZALT** with any other drug in the same class (Triptans) within 24 hours, such as sumatriptan, naratriptan, zolmitriptan, or eletriptan.
- Do not take **RIZALT** within 24 hours of taking ergotamine containing medicines, such as ergotamine, dihydroergotamine, or methysergide to treat your migraine.
- Do not take **RIZALT** when you are taking antidepressant drugs from the monoamine oxidase (MAO) inhibitors group, such as moclobemide, isocarboxazid, phenelzine or tranylcypromine, and pargyline or if it has been less than two weeks since you stopped taking a MAO inhibitor.

Especially inform your doctor or pharmacist if you are taking:

- propranolol containing medicines (See section 3 "HOW SHOULD YOU USE **RIZALT**?").
- medicines used to treat mood disorders, including medicines from the group of selective serotonin re-uptake inhibitors (SSRIs) such as fluoxetine, fluvoxamine, paroxetine, ecitalopram oxalate and sertraline or serotonin norepinephrine reuptake inhibitors (SNRIs), such as venlafaxine and duloxetine for depression.

2.4 Using RIZALT with food and drink
RIZALT can take longer to work if it is taken after food. Although it is better to take it on an empty stomach, you can still take it if you have eaten.

2.5 Pregnancy and breast-feeding
It is not known whether **RIZALT** is harmful to an unborn baby when taken by a pregnant woman.

Talk to your doctor before taking this medicine if you are pregnant or planning to become pregnant.
It is not known if **RIZALT** passes into breast milk. If you are breast-feeding or plan to breast-feed, consult your doctor. Breast-feeding should be avoided for 24 hours after treatment.

Consult your doctor or pharmacist before taking any medicine.

2.6 Driving or using machines
RIZALT may cause dizziness, sleepiness, tiredness, weakness or fainting. If you have these symptoms, do not drive a car, operate machinery, or engage in any other activity which requires alertness.

2.7 Important information about some of the ingredients of RIZALT Tablets and RIZALT RPD Wafers
RIZALT 10 mg tablets:. The 10 mg tablet contains 60.50 mg of lactose monohydrate. Inform your physician if you suffer from lactose intolerance.

RIZALT 10 mg RPD Wafers: This medicine contains 3.75mg aspartame in each **RIZALT 10mg RPD Wafer** which is equivalent to 2.1mg phenylalanine.
Aspartame is a source of phenylalanine. It may be harmful if you have phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.

3. HOW SHOULD YOU USE RIZALT?
Always take **RIZALT** according to the doctor's instructions. You should check with your doctor or pharmacist if you are not sure regarding the dosage and treatment regimen.
The dosage and treatment regimen will be determined by the doctor only.
Do not exceed the recommended dose.
The maximum dosage is 30 mg **RIZALT** in any 24-hour period. Do not take more than 30 mg of **RIZALT** in a 24-hour period (for example, do not take more than three 10 mg tablets or wafers in a 24-hour period).

SOME PATIENTS SHOULD RECEIVE A LOWER DOSE OF RIZALT, IN PARTICULAR THE FOLLOWING PATIENT GROUPS:

- Patients taking propranolol
- Moderate to severe hepatic impairment
- Renal impairment
- Elderly patients

If lower dose is not optional, the physician should consider alternative therapies for these patients, for example, other 5-$HT_{1B/1D}$ agonists.
This medicine is not intended for administration to children and adolescents under 18 years of age.
Most migraine attacks are relieved with **RIZALT**. However, in some patients, migraine symptoms can return within a 24-hour period. If your migraine does return you can take an additional dose of **RIZALT**. You should always wait at least 2 hours between doses.
If you do not respond to **RIZALT** during an attack, it is recommended that you do not take **RIZALT** for treatment of the same attack. It is still likely, however, that you will respond to **RIZALT** during the next attack.

DIRECTIONS FOR USE:
RIZALT Tablets: The tablet should be swallowed whole with liquid. There is no information regarding crushing/splitting/chewing of the tablets.

RIZALT RPD Wafers: Leave the RPD wafer in its package until you are ready to take it. Do not remove the blister from the outer foil pouch until just prior to dosing.

- Remove the blister from the foil pouch. Do not push the RIZALT RPD wafer through the blister.
- Peel open the blister pack with dry hands and place the wafer on the tongue, where it will dissolve rapidly and be swallowed with your saliva. Administration with liquid is not necessary. The wafer can be taken without regard to meals.

If you take more RIZALT than you should:
If you take more **RIZALT** than you should, contact your doctor immediately or go to the nearest hospital emergency room right away.

If you have taken an overdose, or if a child has accidentally swallowed the medicine, proceed immediately to a hospital emergency room and bring the package of the medicine with you.

Do not take medicines in the dark! Check the label and the dose <u>each time</u> you take your medicine. Wear glasses if you need them.

If you have further questions regarding the use of this medicine consult with your doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, **RIZALT** may cause side effects, in some of the users.
Do not be alarmed by reading the list of side effects, you may not suffer from any of them.

Refer to the doctor or go to the nearest hospital emergency room right away, if you develop any of the serious side effects of RIZALT including:

- **heart attack.** Symptoms of a heart attack may include:
    - chest discomfort in the center of your chest that lasts for more than a few minutes or that goes away and comes back
    - chest discomfort that feels like uncomfortable pressure, squeezing, fullness or pain
    - pain or discomfort in your arms, back, neck, jaw or stomach
    - shortness of breath with or without chest discomfort
    - breaking out in a cold sweat
    - nausea or vomiting
    - feeling lightheaded

- **stroke.** Symptoms of a stroke may include the following sudden symptoms:
    - numbness or weakness in your face, arm or leg, especially on one side of your body
    - confusion, problems speaking or understanding
    - problems seeing in one or both of your eyes
    - problems walking, dizziness, loss of balance or coordination
    - severe headache with no known cause

- **blood vessel problems.** Symptoms of blood vessel problems may include:
    - stomach pain
    - bloody diarrhea
    - vision problems
    - coldness and numbness of hands and feet

- **serotonin syndrome.** A condition called serotonin syndrome can happen when Triptan medicines such as **RIZALT** are taken with certain other medicines. Symptoms of serotonin syndrome may include:

    - agitation
    - hallucinations
    - coma
    - fast heartbeat
    - fast changes in your blood pressure
    - increased body temperature
    - muscle spasm
    - loss of coordination
    - nausea, vomiting or diarrhea

- **increased blood pressure**.

- **Allergic reactions** including swelling of face, lips, tongue and/or throat which may cause difficulty in breathing and/or swallowing, wheezing, hives, rash, and severe sloughing of the skin.
- In addition, tell your doctor if you experience any symptoms that suggest an allergic reaction (such as a rash or itching) after taking **RIZALT**.

Additional side effects:
The most **common** side effects of **RIZALT** include:
- feeling sleepy or tired
- pain or pressure in your chest or throat
- dizziness

Other side effects (Common: 1 to 10 in 100 patients; Uncommon: from 1 to 10 in 1000 patients; rare: 1 to 10 in 10,000 patients); and side effects with unknown frequency (side effects for which frequency has not been determined yet):

Immune system disorders: *Rare:* allergic reaction (hypersensitivity), sudden life-threatening allergic reaction (anaphylaxis).
Gastrointestinal disorders: *common:* feeling sick (nausea), vomiting, diarrhea, dry mouth; *uncommon*: thirst, indigestion (dyspepsia).
Respiratory, thoracic and mediastinal disorders: *common:* throat discomfort/pain, difficulty breathing (dyspnoea); *; Rare*: wheezing.
Musculoskeletal and connective tissue disorders: *common:* feelings of heaviness in parts of the body, neck pain; *uncommon*: feeling of tightness in parts of the body, muscle weakness, stiffness, muscle pain and facial pain.
Skin and subcutaneous tissue disorders: *common:* flushing (redness of the face lasting a short time); *uncommon:* sweating, itching, lumpy rash (hives), rash, angioedema (swelling of face, lips, tongue and/or throat which may cause difficulty breathing and/or swallowing).
Cardiac disorders: *common:* fast or irregular heartbeat (palpitation); *uncommon:* very fast heartbeat (tachycardia), changes in the rhythm or rate of the heartbeat (arrhythmia), slow heartbeat (bradycardia); abnormalities of the electrocardiogram (ECG - a test that records the electrical activity of the heart); *rare*: stroke (this generally occurs in patients with risk factors for heart and blood vessel disease (high blood pressure, diabetes, smoking, use of nicotine substitution, family history of heart disease or stroke, man over 40 years of age, postmenopausal women, particular problem with the way your heart beats (bundle branch block)).
Vascular disorders: *uncommon*: high blood pressure (hypertension); *rare*: hot flushes; *Unknown frequency*: peripheral vascular ischaemia.
Nervous system disorders: *common:* dizziness, sleepiness, tingling (paraesthesia), headache, decreased sensitivity of skin (hypoaesthesia), decreased mental sharpness, tremor; *uncommon*: bad taste in your mouth, unsteadiness when walking (ataxia), vertigo; *rare*: fainting (syncope).

Psychiatric disorders: *uncommon*: confusion/disorientation, insomnia.
Eye disorders: *uncommon:* blurred vision.
General disorders and administration site conditions: *common*: pain in abdomen or chest, tiredness.

Reported side effects with unknown frequency (side effects for which frequency has not been determined yet):

- heart attack, spasm of the blood vessels of the heart (these generally occur in patients with risk factors for heart and blood vessel disease (high blood pressure, diabetes, smoking, use of nicotine substitution, family history of heart disease or stroke, man over 40 years of age, postmenopausal women, particular problem with the way your heart beats (bundle branch block)).
- severe shedding of the skin with or without fever (toxic epidermal necrolysis).
- seizure (convulsions/fits).
- a syndrome called "serotonin syndrome" that may cause side effects like coma, unstable blood pressure, extremely high body temperature, lack of muscle coordination, agitation, and hallucinations.
- spasm of blood vessels of the extremities including coldness and numbness of the hands or feet.
- Spasm of the blood vessels of the colon (large bowel), which can cause abdominal pain.
- Visual disorders such as flickering, reduced vision, double vision, loss of vision and in some cases even permanent defects of vision (however these may also occur due to the migraine attack itself).

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

Side effects can be reported to the Ministry of Health by using the link "Adverse Drug Reactions Report" at the home page of the Ministry of Health's web site (www.health.gov.il) which refers to the online side effects reporting form, or by using the link:
https://sideeffects.health.gov.il/

5. HOW TO STORE RIZALT?

- Avoid poisoning! This medicine, as all other medicines, must be stored in a safe place out of the reach and sight of children and/or infants, in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor!
- Do not use **RIZALT** after the expiry date (exp. date) which is stated on pack. The expiry date refers to the last day of the indicated month.
- **Storage conditions**:
  RIZALT 10 mg Tablets and **RIZALT RPD** 10 mg Wafers: Store below 30°C.
- Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

6.1 What RIZALT contains

The active substance of **RIZALT** is rizatriptan (as benzoate).
One **RIZALT** 10 mg tablet contains 10 mg rizatriptan as 14.53 mg of rizatriptan benzoate.
One **RIZALT RPD** 10 mg wafer contains 10 mg rizatriptan as 14.53 mg of rizatriptan benzoate.

The other ingredients of **RIZALT** Tablets are microcrystalline cellulose, lactose monohydrate, pregelatinised starch, magnesium stearate and Ferric oxide (red).
RIZALT 10 mg tablets contain lactose monohydrate, see section 2.7 "Important information about some of the ingredients of **RIZALT** Tablets and **RIZALT RPD** Wafers".

The other ingredients of **RIZALT RPD** 10 mg Wafers are: gelatin, mannitol, glycine, aspartame and peppermint Naefco P.
RIZALT RPD 10 mg Wafers contain aspartame, see section 2.7 "Important information about some of the ingredients of **RIZALT** Tablets and **RIZALT RPD** Wafers".

6.2 What RIZALT looks like and contents of pack
RIZALT 10 mg Tablets: 10 mg tablets are pale pink, capsule-shaped, convex tablets, coded 267 on one side and plain on the other.
RIZALT RPD 10 mg Wafers: 10 mg wafers are white to off-white, round with a flat or slightly irregular surface and a modified square on one side and plain on the other side, with a peppermint flavour. Each orally disintegrating tablet is individually packaged in a blister inside an aluminum pouch (sachet).

Pack sizes: Packs with 2, 3, 6 or 12 tablets or wafers.
Not all pack sizes may be marketed.

Marketing authorization holder:
Merck Sharp & Dohme (Israel-1996) Company Ltd., P.O. Box 7121, Petah-Tikva 49170.

Manufacturer: Merck Sharp and Dohme Corp., New Jersey, USA

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Drug registration no. listed in the official registry of the Ministry of Health:

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