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

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

Reagila® 1.5, 3, 4.5, 6
Capsules

Each capsule contains cariprazine as hydrochloride salt at a dose of 1.5, 3, 4.5 or 6 mg respectively.

Inactive ingredients and allergens in the medicine - see section 6 "Additional information" and in 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 this medicine. If you have any further questions, ask the doctor or pharmacist.
This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if you think that their medical condition is similar to yours.

1. What is the medicine intended for?

Reagila is indicated for the treatment of schizophrenia in adults.

Reagila contains the active ingredient cariprazine and belongs to a group of medicines called antipsychotics.
Schizophrenia is a disease characterized by symptoms such as hearing, seeing or sensing things which are not there (hallucinations), suspiciousness, mistaken beliefs, incoherent speech and behavior and emotional flatness. People with this condition may also feel depressed, guilty, anxious, tense, or not being able to start or keep up planned activities, unwillingness to speak, lack of emotional response to a situation that would normally stimulate feelings in others.

Therapeutic group: antipsychotic medicine.

2. Before using the medicine

Do not use the medicine if:
- You are hypersensitive (allergic) to the active ingredient (cariprazine) or to any of the other ingredients this medicine contains (see section 6).
- You are taking medicines for the treatment of:
  - hepatitis caused by the hepatitis C virus (medicines containing boceprevir, telaprevir)
  - bacterial infections (medicines containing clarithromycin, telithromycin, erythromycin, nafcillin)
  - tuberculosis (medicines containing rifampicin)
  - HIV infections (medicines containing cobicistat, indinavir, nelfinavir, ritonavir, saquinavir, efavirenz, etravirine)
  - fungal infections (medicines containing itraconazole, posaconazole, voriconazole, fluconazole)
  - Cushing's syndrome - when the body produces an excess of cortisol (medicines containing ketoconazole)
  - depression (herbal medicine containing St. John's wort (Hypericum perforatum) and medicines containing nefazodone)
  - epilepsy and seizures (medicines containing carbamazepine, phenobarbital, phenytoin)
  - heart disease (medicines containing diltiazem, verapamil)
  - sleepiness (medicines containing modafinil)
  - high blood pressure in the lungs (medicines containing bosentan)

Special warnings regarding the use of the medicine

Tell your doctor immediately if:
- you are having any thoughts or feelings about hurting yourself or to commit suicide. Suicidal thoughts and behaviors are more likely at the beginning of the treatment.
- you suffer from a combination of fever, sweating, faster breathing, muscle stiffness and drowsiness or sleepiness (may be signs of neuroleptic malignant syndrome).

Before or during the treatment with Reagila, tell the doctor if:
- you have ever suffered or start to suffer from restlessness and inability to sit still. These symptoms may occur early during treatment with **Reagila**. Tell your doctor if this happens.
- you have ever suffered or start to suffer from abnormal, involuntary movements, most commonly of the tongue or face. Tell your doctor if this happens.
- you suffer from visual impairment. Your doctor will advise you to visit an ophthalmologist.
- you suffer from irregular heart beat or if someone else in your family has a history of irregular heart beat (including QT prolongation seen with ECG monitoring), and tell your doctor if you are taking other medicines, because they might cause or worsen this ECG change.
- you suffer from high or low blood pressure, cardiovascular disease. Your doctor will need to check your blood pressure regularly.
- you suffer from dizziness on standing up due to a significant decrease in your blood pressure, which may cause fainting.
- you or if someone else in your family have had blood clots in the past, as medicines for schizophrenia have been associated with formation of blood clots.
- you have a history of stroke, especially if you are elderly or know that you have other risk factors for stroke. Tell your doctor immediately if you notice any signs of a stroke.
- you suffer from dementia (loss of memory and other mental abilities), especially if you are elderly.
- you suffer from Parkinson's disease.
- you suffer from diabetes or risk factors for diabetes (e.g. obesity, or someone else in your family suffers from diabetes). Your doctor will need to check your blood sugar regularly since it may be increased while using **Reagila**. Signs of high blood sugar level are excessive thirst, passing of large amounts of urine, increase in appetite and feeling weak.
- you have ever suffered from seizures (fits) or epilepsy.

Weight increase
Reagila may cause significant weight increase which may affect your health. Therefore, your doctor should check your weight regularly.

Contraception
Women of childbearing age must use highly effective contraception while taking **Reagila** and for at least 10 weeks after stopping treatment. If you are using hormonal contraceptives, a birth control barrier (e.g. condom or diaphragm) should also be used. See section "Pregnancy, breast-feeding and fertility".

Children and adolescents

This medicine is not recommended for children and adolescents under 18 years due to the lack of data in these patients.

Drug interactions

If you are taking, have recently taken or might take other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. You cannot take certain medicines together with **Reagila** (see section 2 "Do not use the medicine if").
Taking **Reagila** together with certain medicines may require a dose adjustment of **Reagila** or the other medicine. These are medicines used to treat heart diseases containing digoxin, blood thinners containing dabigatran, or medicines affecting your mental function.
If you are using hormonal contraceptives, a birth control barrier should also be used (see section "Pregnancy, breast-feeding and fertility").

Use of this medicine and food

Do not drink grapefruit juice during treatment with **Reagila.**

Use of this medicine and alcohol consumption

You should avoid alcohol consumption during treatment with **Reagila.**

Pregnancy, breast-feeding and fertility

Women of childbearing age
Women of childbearing age must use effective contraception during **Reagila** treatment. Even after treatment is stopped, contraception must be used for at least 10 weeks after your last dose of **Reagila**. This is because the medicine will stay in your body for some time after the last dose was taken. If you are using hormonal contraceptives, a birth control barrier (e.g. condom or diaphragm) should also be used. Ask your doctor about appropriate choices of contraception.

Pregnancy
Do not take this medicine during pregnancy unless your doctor has told you to do so.
If your doctor decides that you should take this medicine during pregnancy, your doctor will monitor your baby closely after birth. This is because the following symptoms may occur in newborn babies of mothers who have used this medicine in the last pregnancy trimester (last three months of pregnancy): shaking, muscle stiffness and/or weakness, sleepiness, agitation, breathing problems and difficulty in feeding. If your baby develops any of these symptoms, contact your doctor.

Breast-feeding
Do not breast-feed during treatment with **Reagila** because a risk for the baby cannot be excluded. Contact your doctor for advice.

Driving and using machines

There is a minor or moderate risk that the medicine could affect the ability to drive and use machines. Drowsiness, dizziness and vision problems may occur during using this medicine (see section 4 "Side effects"). Avoid driving or using tools or machines until you know that this medicine does not affect you in a negative way.

Important information about some of the ingredients of the medicine

Reagila 3, 4.5, 6 capsules contains Allura red AC (E 129).
This is a coloring agent, which may cause allergic reactions.

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 not sure about the dosage and the manner of treatment with the medicine.

The dosage and manner of treatment will be determined by the doctor only.

The recommended starting dose is 1.5 mg once a day by mouth. Thereafter, the dose may be gradually adjusted by your doctor, in steps of 1.5 mg, depending on your reaction to the treatment. The maximum dose should not exceed 6 mg once a day.

Do not exceed the recommended dose.

Take **Reagila** at the same time each day, with or without food.

If you were taking another medicine to treat schizophrenia before starting **Reagila**, your doctor will decide whether to stop the other medicine gradually or immediately and how to adjust the dose of **Reagila**. Your doctor will also inform you how to act if you switch from **Reagila** to another medicine.

Patients with kidney or liver problems
If you suffer from serious kidney or liver problems, **Reagila** may not be appropriate for you. Consult your doctor.

Elderly
Your doctor will carefully select the appropriate dose for your needs.
Reagila is not intended for the treatment of the elderly with dementia (loss of memory).

If you have accidentally taken a higher dosage

If you have taken an overdose or if a child has accidentally swallowed the medicine, proceed immediately to a doctor or a hospital emergency room and bring the package of the medicine with you. You may feel dizziness due to low blood pressure, abnormal heartbeats, sleepiness, tiredness, abnormal body movements, difficulty to stand or walk.

If you forgot to take the medicine

If you forgot to take this medicine at the designated time, take the dose as soon as you remember. However, if it is almost time for your next dose, skip the missed dose and continue as usual. Do not take a double dose to make up for a forgotten dose. If you forget to take two or more doses, contact your doctor.

Continue with the treatment as recommended by the doctor.

If you stop taking the medicine

If you stop taking this medicine, the effects of the medicine will expire. Even if there is an improvement in your health, do not alter or stop treatment with **Reagila** without consulting the doctor, as the symptoms may return.

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 further questions on the use of this medicine, consult a doctor or a pharmacist.

4. Side effects

Like any medicine, the use of **Reagila** 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.

Refer to a doctor immediately if you have:
- a severe allergic reaction characterized by fever, swollen mouth, face, lips or tongue, shortness of breath, itching, rash and sometimes a significant decrease in blood pressure. (Rare side effect)
- combination of fever, sweating, muscle stiffness, and drowsiness or sleepiness. These can be the signs of the neuroleptic malignant syndrome. (Side effect with frequency not known)
- inexplicable muscle pains, muscle cramps or muscle weakness. These may be signs of muscle damage which can cause very serious kidney problems. (Rare side effect)
- symptoms related to blood clots in the veins, especially in the legs (symptoms include swelling, pain and redness in the leg), which may travel through blood vessels to the lungs causing chest pain and difficulty in breathing. (Side effect with frequency not known)
- thoughts or feelings about hurting yourself or committing suicide, suicide attempt. (Uncommon side effect)

Additional side effects:
Very common side effects (effects that appear in more than 1 in 10 users):
- Restlessness and inability to sit still
- Parkinsonism - a medical condition with many various symptoms which include decreased or slow movements, slowness of thought, jerks when bending the limbs ("cogwheel" rigidity), shuffling steps, shaking, little or no facial expression, muscle stiffness, drooling

Common side effects (effects that appear in 1-10 out of 100 users):
- anxiety
- sleepiness, difficulty in sleeping, abnormal dreams, nightmare, sleepwalking
- dizziness
- involuntary twisting movements, strange postures
- excessive teeth grinding or jaw clenching, drooling, persistent blinking in response to tapping of the forehead (an abnormal reflex), movement problems, tongue movement disturbance (these are called extrapyramidal symptoms)
- blurred vision
- high blood pressure
- fast, irregular heartbeat
- decreased or increased appetite
- nausea, vomiting, constipation
- weight increased
- tiredness
- effects that can be seen in laboratory tests:
  - increase in liver enzymes
  - increase in the level of creatine phosphokinase in the blood
  - abnormal amount of lipids (e.g. cholesterol and/or fat) in the blood

Uncommon side effects (effects that appear in 1-10 out of 1,000 users):
- depression
- sudden and severe confusion
- spinning sensation
- unpleasant, abnormal sense of touch
- drowsiness, lack of energy or a lack of interest in doing things
- involuntary movements, most commonly of the tongue or face. These effects can appear after short or long term use.
- decreased or increased sexual desire, erectile problems
- eye irritation, high pressure in the eye, poor vision
- focusing problems seeing at a distance to or seeing close-to
- low blood pressure
- abnormal ECG reading, abnormal nerve impulses in the heart
- slow, irregular heart rate
- hiccups
- heartburn
- thirst
- pain when passing urine
- abnormally frequent and large urinations
- itching, rash
- diabetes
- effects that can be seen in laboratory tests:
  - abnormal sodium level in the blood
  - increased blood glucose (blood sugar), increased bile pigment (bilirubin) in the blood
  - anaemia (reduced levels of red blood cells)
  - increase in a certain type of white blood cells
  - decreased level of thyroid stimulating hormone (TSH) in the blood

Rare side effects (effects that appear in 1-10 out of 10,000 users):
- seizure
- loss of memory, loss of speech
- eye discomfort in bright light
- clouding of the lens in the eye, leading to a decrease in vision (cataract)
- difficulty in swallowing
- reduced levels of a certain type of white blood cells, this can make you more susceptible to infections
- underactive thyroid gland

Side effects with unknown frequency (effects for which a frequency has not yet been determined):
- inflammation of the liver (pain in the upper right abdomen, yellowing of the eye and skin, weakness, fever)

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

Side effects can be reported to the Ministry of Health via the link "דיווח על תופעות 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://sideeffects.health.gov.il

5. How to store the medicine

- Avoid poisoning! This medicine and any other medicine must be stored in a closed 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.) stated on the package. The expiry date refers to the last day of that month.
- **Storage conditions:** store below 25°C in the outer package in order to protect from light.
- 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:

Reagila 1.5:
Starch pregelatinized (maize), gelatine, titanium dioxide (E 171), magnesium stearate, black ink (black iron oxide (E 172), shellac, propylene glycol, potassium hydroxide)

Reagila 3:
Starch pregelatinized (maize), gelatine, magnesium stearate, titanium dioxide (E 171), yellow iron oxide (E 172), brilliant blue FCF (E 133), allura red AC (E 129), black ink (black iron oxide (E 172), shellac, propylene glycol, potassium hydroxide)

Reagila 4.5:
Starch pregelatinized (maize), gelatine, magnesium stearate, titanium dioxide (E 171), yellow iron oxide (E 172), brilliant blue FCF (E 133), allura red AC (E 129), white ink (shellac, titanium dioxide (E 171), propylene glycol, simeticone)

Reagila 6:
Starch pregelatinized (maize), gelatine, titanium dioxide (E 171), magnesium stearate, allura red AC (E 129), brilliant blue FCF (E 133), black ink (black iron oxide (E 172), shellac, propylene glycol, potassium hydroxide)

What the medicine looks like and what the package contains:

Reagila 1.5: White capsule imprinted with "GR 1.5" in black ink. Approved package sizes: 14 or 30 capsules.
Reagila 3: Green and white capsule imprinted with "GR 3" in black ink. Approved package sizes: 14 or 30 capsules.
Reagila 4.5: Green capsule imprinted with "GR 4.5" in white ink. Approved package size: 30 capsules.
Reagila 6: Purple and white capsule imprinted with "GR 6" in black ink. Approved package size: 30 capsules.
Not all package sizes may be marketed.

Manufacturer and his address: Gedeon Richter Plc., Budapest, Hungary.

Revised in May 2020.

Drug registration number at the national drug registry of the Ministry of Health:

Reagila 1.5: 163-54-35920-00
Reagila 3: 163-55-35921-00
Reagila 4.5: 163-56-35922-00
Reagila 6: 163-57-35923-00

Reagila 1.5, 3, 4.5, 6 PIL PB0420-08

Registration holder: Dexcel® Ltd.
1 Dexcel St., Or Akiva 3060000, Israel