1.3.2 Patient Information Leaflet for Reagila.

SCHEDULING STATUS

S5

Reagila 1,5 mg hard capsules

Reagila 3 mg hard capsules

Reagila 4,5 mg hard capsules

Reagila 6 mg hard capsules

Cariprazine hydrochloride

Sugar free.

Read all of this leaflet carefully before taking Reagila.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- Reagila has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What Reagila is and what it is used for

Reagila contains the active substance cariprazine and belongs to a group of medicines called antipsychotics. It is used to treat adults with schizophrenia.

Schizophrenia is a disease characterised by symptoms such as hearing, seeing or sensing things which are not there (hallucination), suspiciousness, mistaken beliefs, incoherent speech and behaviour 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.

2. What you need to know before you take Reagila

You should not take Reagila

- if you are allergic to cariprazine or any of the other ingredients of this medicine (listed in section 6).
- if you are taking medicines used to treat:
  - hepatitis caused by the hepatitis C virus (medicines containing boceprevir and telaprevir)
  - bacterial infections (medicines containing clarithromycin, telithromycin, erythromycin and nafcillin)
  - tuberculosis (medicines containing rifampicin)
  - HIV infections (medicines containing cobicistat, indinavir, nelfinavir, ritonavir, saquinavir, efavirenz and etravirine)
  - fungal infections (medicines containing itraconazole, posaconazole, voriconazole, fluconazole and ketoconazole)
  - depression (herbal therapy containing St. John's wort (*Hypericum perforatum*) and medicines containing nefazodone)
  - epilepsy and seizures (medicines containing carbamazepine, phenobarbitone and phenytoin)
  - heart disease (medicines containing diltiazem and verapamil)
  - sleepiness (medicines containing modafinil)

- high blood pressure in the lungs (medicines containing bosentan).
- if you are pregnant, breastfeeding or planning to become pregnant.

Warnings and precautions:

Tell your doctor immediately:

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

Talk to your doctor or pharmacist before taking Reagila, or during treatment if you have:

- ever experienced or start to experience restlessness and inability to sit still. These symptoms may occur early during treatment with Reagila. Tell your doctor if this happens.
- ever experienced or start to experience abnormal, involuntary movements, most commonly of the tongue or face. Tell your doctor if this happens.
- visual impairment. Your doctor will advise you to visit an ophthalmologist.
- irregular heart beat or if someone else in your family has a history of irregular heart beat (including so called 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.
- high or low blood pressure, cardiovascular disease. Your doctor will need to check your blood pressure regularly.
- dizziness on standing up due to a drop in your blood pressure, which may cause fainting.
- a history of blood clots, or if someone else in your family has a history of blood clots, as medicines for schizophrenia have been associated with formation of blood clots.
- 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.
- dementia (loss of memory and other mental abilities) especially if you are elderly.
- Parkinson’s disease.
- if you have diabetes or risk factors for diabetes (e.g. obesity, or someone else in your family

has diabetes). Your doctor will need to check your blood sugar regularly since it may be increased by Reagila. Signs of high blood sugar level are excessive thirst, passing of large amounts of urine, increase in appetite and feeling weak.

- a history of seizures (fits) or epilepsy.

Weight increase

Reagila may cause significant weight increase which may affect your health. Your doctor will therefore check your weight regularly.

Contraception

Women of childbearing potential must use highly effective contraception while taking Reagila and for at least 10 weeks after stopping treatment. If you are using hormonal contraceptives a so-called barrier method (e.g. condom or diaphragm) should also be used (see section “Pregnancy and breastfeeding”).

Children and adolescents

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

Other medicines and Reagila:

Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicines.)

Taking Reagila together with some 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 functions.

If you are using hormonal contraceptives a so-called barrier method should also be used (see section “Pregnancy and breastfeeding”).

Reagila with food, drink and alcohol

You should not drink grapefruit juice during treatment with Reagila. Alcohol should be avoided when taking Reagila.

Pregnancy and breastfeeding:

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before using Reagila.

Women of childbearing potential

Women of childbearing potential 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 Reagila will stay in your body for some time after the last dose was taken. If you are using hormonal contraceptives a so-called barrier method (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.

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 trimester (last three months) of their pregnancy:

- shaking, muscle stiffness and/or weakness, sleepiness, agitation, breathing problems, and difficulty in feeding.

If your baby develops any of these symptoms you should contact your doctor.

Driving and using machines

There is a risk that the medicine could affect the ability to drive and use machines. Drowsiness, dizziness and vision problems may occur during treatment with Reagila (see section 4). Do not drive or use any tools or machines until you know that this medicine does not affect you in a negative way.

Reagila 3 mg, 4.5 mg, 6 mg hard capsules contain Allura red AC

Allura red AC is a colourant, which may cause allergic reactions.

3. How to take Reagila

Do not share medicines prescribed for you with any other person. Always use Reagila exactly as your doctor has instructed you.

The recommended starting dose is 1,5 mg once a day by mouth. Thereafter, the dose may be slowly adjusted by your doctor, in steps of 1,5 mg, depending on how the treatment works for you.

The maximum dose should not exceed 6 mg once a day.

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.

If you have the impression that the effect of this medicine is too strong or too weak, talk to your doctor.

If you take more Reagila than you should

If you used too much of Reagila, or if, for example, a child has taken it by mistake contact your doctor or pharmacist straight away. If neither is available, seek help at the nearest hospital or poison control centre. You may experience dizziness from low blood pressure, or have abnormal heartbeats, you may feel sleepy, tired, or have abnormal body movements and find it difficult to stand or walk.

If you forget to take Reagila

If you forget to take a dose, take it as soon as you remember it. 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 miss two or more doses, contact your doctor.

If you stop taking Reagila

If you stop taking Reagila you will lose the effects of the medicine. Even if you feel better, do not alter or stop your daily dose of Reagila unless told to do so by your doctor as your symptoms may return.

4. Possible side effects

Reagila can have side effects.

Not all side effects reported for Reagila are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking Reagila, please consult your doctor, pharmacist or other healthcare professional for advice.

If any of the following happens, stop using Reagila and tell your doctor immediately or go to the casualty department at your nearest hospital:

- difficulty breathing
- chest tightness

- swelling of the face
- rash or hives.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to Reagila. You may need urgent medical attention or hospitalisation.

Tell your doctor **immediately** or go to the casualty department at your nearest hospital if you notice any of the following:

- a severe allergic reaction seen as fever, swollen mouth, face, lip or tongue, shortness of breath, itching, skin rash and sometimes a drop in blood pressure.
- combination of fever, sweating, muscle stiffness, and drowsiness or sleepiness. These can be the signs of the so-called neuroleptic malignant syndrome.
- inexplicable muscle pains, muscle cramps or muscle weakness. These may be signs of muscle damage which can cause very serious kidney problems.
- 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.
- thoughts or feelings about hurting yourself or to commit suicide, suicide attempt.

Tell your doctor if you notice any of the following:

Frequent side effects

- feeling of 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
- anxiety
- sleepiness, difficulty in sleeping, abnormal dreams, nightmare, sleepwalking
- dizziness
- involuntary twisting movements and 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
- the following can be seen in laboratory tests:
  - increases in liver enzymes
  - increases in the level of creatine phosphokinase in the blood
  - abnormal amount of lipids (e.g. cholesterol and/or fat) in the blood

Less frequent side effects

- 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. This 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 and irregular heart rate
- hiccups

- heartburn
- thirst
- pain when passing urine
- abnormally frequent and large urinations
- itching, rash
- diabetes
- the following 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 type of white blood cells
  - decreased level of thyroid stimulating hormone (TSH) in the blood
- 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 type of white blood cells, this can make you more susceptible to infections
- underactive thyroid gland

Side effects with frequency not known

- inflammation of the liver (pain in the upper right abdomen, yellowing of the eye and skin, weakness, fever)

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects:

If you get side effects, talk to your doctor or pharmacist. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

By reporting side effects, you can help provide more information on the safety of Reagila.

5. How to store Reagila

Keep this medicine out of sight and reach of children.

Store at or below 25 °C.

Keep the blister in the outer carton in order to protect from light.

Do not use Reagila after the expiry date which is stated on the carton and the blister after EXP. The expiry date refers to the last day of that month.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What Reagila contains:

The active substance is cariprazine.

Reagila 1,5 mg hard capsules: Each hard capsule contains cariprazine hydrochloride corresponding to 1,5 mg cariprazine.

Reagila 3 mg hard capsules: Each hard capsule contains cariprazine hydrochloride corresponding to 3 mg cariprazine.

Reagila 4,5 mg hard capsules: Each hard capsule contains cariprazine hydrochloride corresponding to 4,5 mg cariprazine.

Reagila 6 mg hard capsules: Each hard capsule contains cariprazine hydrochloride corresponding to 6 mg cariprazine.

The other ingredients are:

Reagila 1,5 mg hard capsules: pregelatinized (maize) starch, magnesium stearate, titanium dioxide (E 171), gelatin, black ink (shellac, black iron oxide (E 172), propylene glycol, potassium hydroxide).

Reagila 3 mg hard capsules: pregelatinized (maize) starch, magnesium stearate, Allura red AC (E 129), brilliant blue FCF (E 133), titanium dioxide (E 171), yellow iron oxide (E 172), gelatin, black ink (shellac, black iron oxide (E 172), propylene glycol, potassium hydroxide).

Reagila 4,5 mg hard capsules: pregelatinized (maize) starch, magnesium stearate, Allura red AC (E 129), brilliant blue FCF (E 133), titanium dioxide (E 171), yellow iron oxide (E 172), gelatin, white ink (shellac, titanium dioxide (E 171), propylene glycol, simeticone).

Reagila 6 mg hard capsules: pregelatinized (maize) starch, magnesium stearate, brilliant blue FCF (E 133), Allura red AC (E 129), titanium dioxide (E 171), gelatin, black ink (shellac, black iron oxide (E 172), propylene glycol, potassium hydroxide).

What Reagila looks like and contents of the pack:

Reagila 1,5 mg hard capsules: 'Size 4' (approximately 14,3 mm in length) hard gelatin capsule with white opaque cap and white opaque body imprinted with "GR 1.5" on the capsule body with black ink. The capsules are filled with white to yellowish white powder.

Reagila 3 mg hard capsules: 'Size 4' (approximately 14,3 mm in length) hard gelatin capsule with green opaque cap and white opaque body imprinted with "GR 3" on the capsule body with black ink. The capsules are filled with white to yellowish white powder.

Reagila 4,5 mg hard capsules: 'Size 4' (approximately 14,3 mm in length) hard gelatin capsule with green opaque cap and green opaque body imprinted with "GR 4.5" on the capsule body with white ink. The capsules are filled with white to yellowish white powder.

Reagila 6 mg hard capsules: 'Size 3' (approximately 15,9 mm in length) hard gelatin capsule with purple opaque cap and white opaque body imprinted with "GR 6" on the capsule body with black ink. The capsules are filled with white to yellowish white powder.

The capsules are packed in transparent hard PVC/PE/PVDC blister heat-sealed with hard aluminium foil. The blisters are packed in an outer carton.

Reagila 1,5 mg and Reagila 3 mg hard capsules are available in pack sizes containing 7, 14, 21, 28, 30, 49, 56, 60, 84, 90 or 98 hard capsules.

Reagila 4,5 mg and Reagila 6 mg hard capsules are available in pack sizes containing 21, 28, 30, 49, 56, 60, 84, 90 or 98 hard capsules.

Not all pack sizes may be marketed.

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This leaflet was last revised in:

19 July 2022.

Registration numbers:

55/2.6.5/0097

55/2.6.5/0098

55/2.6.5/0099

55/2.6.5/0100