

SYMVENU® HARD CAPSULES

Cariprazine (1.5mg, 3mg, 4.5mg, 6mg)

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What SYMVENU is used for

SYMVENU 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.
- for short-term (acute) treatment of manic or mixed episodes that happen with bipolar I disorder.

The duration of the treatment depends on the clinical response and tolerability, and should be determined based on the clinical judgement of the treating physician.

- to treat depressive episodes that happen with bipolar I disorder. Bipolar I disorder is a condition that causes periods of severe changes in your mood, activity levels, energy, and ability to carry out everyday tasks. These changes are commonly called "mood episodes."
- along with antidepressant medicines to treat major depressive disorder (MDD)

Depression is a mood disorder that causes a persistent feeling of sadness and loss of interest. Also called major depressive disorder or clinical depression, it affects

how you feel, sleep, your appetite, behave and ability to think clearly. You may have trouble doing normal day-to-day activities, and sometimes you may feel as if life isn't worth living.

How SYMVENU works

The mechanism of action of cariprazine is not fully known. However, the therapeutic effect of cariprazine may be mediated through a combination of partial agonist activity at dopamine D₃, D₂ and serotonin 5-HT_{1A} receptors, and antagonist activity at serotonin 5-HT_{2B}, 5-HT_{2A} and histamine H₁ receptors.

Before you use SYMVENU

- When you must not use it

Do not take this medicine if:

- you are allergic to cariprazine or any other ingredients of this medicine (listed in Product Description)
- 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 and nafcillin)
 - tuberculosis (medicines containing rifampicin)
 - HIV infections (medicines containing cobicistat, indinavir, nelfinavir, ritonavir, saquinavir, efavirenz and etravirine)
 - fungal infections (medicines containing itraconazole, posaconazole and voriconazole)
 - Cushing's syndrome - when the body produces an excess of cortisol (medicines containing ketoconazole)
 - depression (herbal therapy containing St. John's wort (*Hypericum perforatum*) and medicines containing nefazodone)
 - epilepsy and seizures (medicines containing carbamazepine, phenobarbital and phenytoin)
 - sleepiness (medicines containing modafinil)
 - high blood pressure in the lungs (medicines containing bosentan).

Children and adolescents

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

- Before you start to use it

Check with your doctor or pharmacist before taking SYMVENU, if you have:

- ever experienced or start to experience restlessness and inability to sit still. These symptoms may occur early during treatment with SYMVENU. 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 should check

your blood sugar before you start taking SYMVENU and regularly during treatment since your blood sugar may be increased by SYMVENU. 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

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

Pregnancy and lactation

Please consult your doctor or pharmacist if you are pregnant, planning for pregnancy or breast-feeding before using any medicine.

- Taking other medicines

Tell your doctor if you are taking any other medicines, including any that you buy without a prescription from a pharmacy, supermarket or health food shop. You cannot take certain medicines together with SYMVENU (see section "When you must not use it").

Taking SYMVENU together with some medicines may require a dose adjustment of SYMVENU or the other medicine. Inform your doctor or pharmacist if you are taking medicines used for the treatment of:

- heart diseases (e.g. digoxin, verapamil, diltiazem),
- blood clotting (blood thinners, e.g. dabigatran),
- bacterial infections (e.g. erythromycin),
- fungal infections (e.g. fluconazole).

SYMVENU should be used with caution in combination with other medicines affecting your mental functions.

If you are using hormonal contraceptives a so-called barrier method should also be used (see section "While you are using it").

How to use SYMVENU

Follow all directions given to you by your doctor and pharmacist carefully. They

may differ from the information contained in this leaflet. If you do not understand the instructions on the label, ask your doctor or pharmacist for help.

- How much to use

Schizophrenia

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.

Manic or mixed episodes associated with Bipolar I Disorder

The recommended starting dose is 1.5 mg once a day by mouth. On the next day this dose should be increased to 3 mg. Depending on how the treatment works for you the dose can be slowly adjusted by your doctor. The maximum dose should not exceed 6 mg once a day.

Depressive episodes associated with bipolar I disorder (bipolar depression)

The recommended starting dose is 1.5 mg once a day by mouth. Depending on how the treatment works for you after two weeks this dose can be increased by your doctor to 3 mg. The maximum dose should not exceed 3 mg once a day.

Adjunctive therapy to antidepressants for the treatment of major depressive disorder

The recommended starting dose is 1.5 mg once daily by mouth. Depending on how the treatment works for you after two weeks this dose can be increased by your doctor to 3 mg. The maximum dose should not exceed 3 mg once a day.

Take SYMVENU at the same time each day with or without food.

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

Patients with kidney or liver problems

If you have serious kidney or liver problems SYMVENU may not be appropriate for you. Talk to your doctor.

Elderly patients

Your doctor will carefully select the appropriate dose for your needs. SYMVENU should not be used by elderly patients with dementia (loss of memory).

- When to use it

Use as directed by your doctor or pharmacist.

- How long to use it

Use this medicine for the duration that your doctor recommends.

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

If you have any further questions on the use of this medicine, ask your doctor.

- If you forget to use it

Take the missed dose as soon as you remember. If it is almost time for your next dose, wait until then to take the medicine and skip the missed dose. Do not take a double dose to make up for the missed dose.

If you miss two or more doses, contact your doctor.

- If you use too much (overdose)

Contact your doctor immediately or go to the Emergency Department of your nearest hospital, if you or anyone else may have used too much of this medicine. Do this even if there are no signs of discomfort or poisoning. You may need urgent medical attention.

Taking too much of this medicine may cause 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.

While you are using SYMVENU

- Things you must do

Use your medicine exactly as your doctor has told you.

Tell all the doctors, dentists and pharmacists treating you that you are using SYMVENU.

Take SYMVENU only with a doctor's prescription.

- Things you must not do

SYMVENU with food, drink and alcohol
You should not drink grapefruit juice during treatment with SYMVENU. Alcohol should be avoided when taking SYMVENU.

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 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.

Breast-feeding

Do not breast-feed if you are taking SYMVENU because a risk for the baby cannot be excluded. Contact your doctor for advice.

Do not stop using the medicine unless advised by your doctor.

Do not use any new medicines without consulting your doctor or pharmacist.

Do not give SYMVENU to anyone else, even if they have the same symptoms or condition as you.

- Things to be careful of

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).

Driving and using machines

This medicine may affect your ability to drive or use machines. Drowsiness, dizziness and vision problems may occur during treatment with this medicine (see 'side effects'). Do not drive or use any tools or machines until you know that this medicine does not affect you in a negative way.

SYMVENU 3 mg, 4.5 mg, 6 mg hard capsules contain Allura red AC (E129).
Allura red AC is a colouring agent, which may cause allergic reactions.

Side effects

Like all medicines, SYMVENU can cause side effects, although not everybody gets them.

Tell your doctor **immediately** if you have:

- 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. (*Rare side effect*)
- combination of fever, sweating, muscle stiffness, and drowsiness or sleepiness. These can be the signs of the so-called 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 to commit suicide, suicide attempt. (*Uncommon side effect*)

Talk to your doctor or pharmacist if you experience:

- increases in blood sugar level and/or symptoms of high blood sugar (e.g. increased thirst, increased hunger, and frequent urination)
- feeling of restlessness and inability to sit still, and an intense urge to move the legs (restless legs syndrome)
- trouble breathing during sleep (sleep apnoea)
- difficulty or inability to pass urine (urinary retention)

Other side effects

Schizophrenia

Very common side effects (may affect more than 1 in 10 people)

- 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 (may affect up to 1 in 10 people)

- 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

Manic or mixed episodes associated with Bipolar I Disorder

Very common side effects (may affect more than 1 in 10 people)

- 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 (may affect more than 1 in 10 people)

- movement problems or uncontrollable movement (extrapyramidal symptoms)
- dyspepsia
- vomiting
- somnolence
- headache
- dry mouth
- musculoskeletal pain
- anxiety
- weight increased
- decreased appetite
- difficulty in sleeping, nightmare
- involuntary twisting movements and strange postures
- dizziness
- blurred vision
- fast, irregular heartbeat
- nausea
- constipation
- tiredness
- high blood pressure
- low blood pressure

Depressive episodes associated with bipolar I disorder (bipolar depression)

Common side effects (may affect more than 1 in 10 people)

- nausea
- restlessness
- movement problems or uncontrollable movement (extrapyramidal symptoms)
- increased appetite
- weight increased
- difficulty in sleeping
- anxiety
- sedation
- dizziness
- vomiting
- musculoskeletal pain

Adjunctive therapy to antidepressants for the treatment of major depressive disorder

Very common side effects (may affect more than 1 in 10 people)

- feeling of restlessness and inability to sit still

Common side effects (may affect up to 1 in 10 people)

- weight increased
- increased appetite
- disturbance in attention, memory impairment, thinking abnormal
- difficulty in sleeping
- anxiety
- excessive sleeping, sleepiness, somnolence
- dizziness
- Parkinsonism - a medical condition with many various symptoms which include decreased or slow movements, shuffling steps, shaking, muscle and joint stiffness
- headache
- involuntary twisting movements and strange postures
- blurred vision
- constipation, nausea, dry mouth
- excessive sweating
- tiredness

Visit your doctor or pharmacist immediately if you experience any side effects after using this medicine.

You may report any side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by visiting the website npra.gov.my [Consumers → Reporting Side Effects to Medicines (ConSERF) or Vaccines (AEFI)].

Storage and Disposal of SYMVENU

- Storage

Keep out of the reach and sight of children.

Do not use this medicine 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.

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

Do not store above 30°C.

- Disposal

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

Product Description

- What it looks like

Symvenu 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.

Symvenu 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.

Symvenu 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.

Symvenu 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 backing. The blisters are packed in a folded carton box.

Symvenu 1.5 mg, 3 mg, 4.5 mg, 6 mg hard capsules are available in pack size containing 28 hard capsules.

- Ingredients

- Active ingredient

The active substance is cariprazine.

Symvenu 1.5 mg: Each hard capsule contains cariprazine hydrochloride corresponding to 1.5 mg cariprazine.

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

Symvenu 4.5 mg: Each hard capsule contains cariprazine hydrochloride corresponding to 4.5 mg cariprazine.

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

- Inactive ingredients

Symvenu 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).

Symvenu 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).

Symvenu 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).

Symvenu 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).

- MAL number(s):

Symvenu 1.5 mg hard capsules:
MAL20086001AZ

Symvenu 3 mg hard capsules:
MAL20086002AZ

Symvenu 4.5 mg hard capsules:
MAL20086003AZ

Symvenu 6 mg hard capsules:
MAL20086004AZ

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Product Registration Holder

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