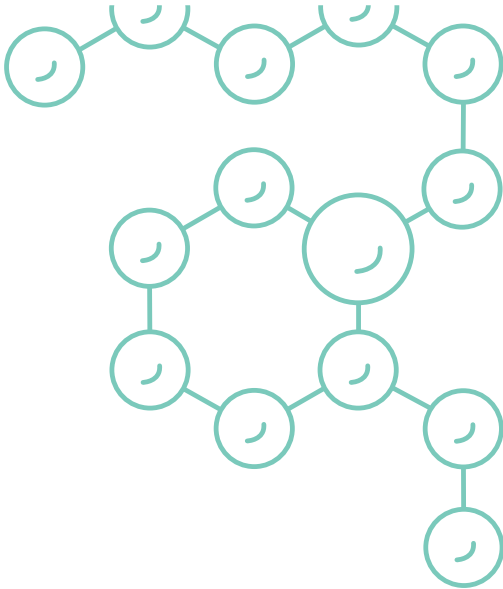




VAPRENA® (Tolvaptan)

Patient Brochure

Risks associated with the use of the product



This document has been reviewed and approved by Saudi Food and Drug Authority (SFDA)

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www.spimaco.sa

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1. What is the purpose of this brochure?

SPIMACO provides this patient education brochure for patients who are being treated with Tolvaptan.

This brochure will:

- explain what Tolvaptan is, what medical condition it is used for and how it should be used
- provide important safety information
- help you to understand potential side effects of Tolvaptan and what to do if they occur

This brochure provides some important information about Tolvaptan. Please read the patient information leaflet found in the medicine package for more details and consult your doctor if you have any questions about your treatment with Tolvaptan.

2. What is Vaprena® (Tolvaptan)?

Tolvaptan, which contains the active substance tolvaptan, belongs to a group of medicines called vasopressin antagonists.

Tolvaptan is used to treat low serum sodium levels in adults. You have been prescribed this medicine because you have a lowered sodium level in your blood as a result of a disease called "syndrome of inappropriate antidiuretic hormone secretion" (SIADH) where the kidneys retain too much water. This disease causes an inappropriate production of the hormone vasopressin which has caused the sodium levels in your blood to get too low (hyponatremia). That can lead to difficulties in concentration and memory, or in keeping your balance.

Vasopressin hormone is involved in the formation of cysts in the kidneys of ADPKD patients. By blocking the effect of vasopressin, Tolvaptan slows the development of kidney cysts in patients with ADPKD, reduces symptoms of the disease and increases urine production.

Tolvaptan is a medicine used to treat a disease called "autosomal dominant polycystic kidney disease" (ADPKD). This disease causes growth of fluid-filled cysts in the kidneys, which puts pressure on surrounding tissues and reduces kidney function, possibly leading to kidney failure. Tolvaptan is used to treat ADPKD in adults with chronic kidney disease (CKD) stages 1 to 4 with evidence of rapidly progressing disease.

3. Which patients are not eligible for treatment with Tolvaptan?

You should not take Tolvaptan if any of the following apply to you:

- If you are allergic to tolvaptan or any of the other ingredients of this medicine including lactose or benzazepine derivatives.
- If you have been told that you have raised levels of liver enzymes in your blood which do not allow treatment with tolvaptan
- If your kidneys do not work (no urine production).
- If you have a condition which increases the salt in your blood ("hypernatremia").
- If you have a condition which is associated with a very low blood volume (e.g. severe dehydration or bleeding).
- If you do not realize when you are thirsty.
- If you are pregnant.
- If you are breast-feeding.

4. Which patients should take special care when taking Tolvaptan?

You should be careful while taking Tolvaptan and tell your doctor if any of the following apply to you:

- you suffer from liver disease
- you cannot drink enough water, you have to limit your fluid intake or you are at an increased risk of water loss
- you have an enlarged prostate or have difficulty urinating
- you suffer from too high or too low blood sodium
- you have diabetes
- you have high levels of uric acid in your blood (which may have caused gout)
- If you have been told by your doctor that you have an intolerance to some sugars

Please ask your doctor if you are not sure if any of these apply to you.

5. How should I take Tolvaptan?

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

In case of using Vaprena for correction of hyponatremia:

Treatment with Tolvaptan will be initiated in hospital.

For treatment of your low sodium (hyponatremia), your doctor will start with a dose of 15 mg and may then increase it to a maximum of 60 mg to achieve the desired level of serum sodium. To monitor the effects of Tolvaptan your doctor will do regular blood tests. To achieve the desired level of serum sodium your doctor can give in some instances a lower dose of 7.5 mg.

Swallow the tablet without chewing, with a glass of water.

Take the tablets once a day preferably in the morning with or without food.

In case of using Vaprena for autosomal dominant polycystic kidney disease ADPKD:

Tolvaptan can be prescribed by doctors who are specialized in the treatment of ADPKD.

Dose

The daily amount of Vaprena is split into two doses, one bigger than the other. The higher dose should be taken in the morning when you wake up, at least 30 minutes before the morning meal. The lower dose is taken 8 hours later.

The dose combinations are:

45 mg + 15 mg

60 mg + 30 mg

90 mg + 30 mg

Your treatment will normally start with a dose of 45 mg in the morning and 15 mg 8 hours later. Your doctor may gradually increase your dose up to a maximum combination of 90 mg on waking and 30 mg after 8 hours. To find the best dose your doctor will regularly check how well you are tolerating a prescribed dose. You should always take the highest tolerable dose combination prescribed by your doctor.

If you take other medicines, which can increase the effects of Tolvaptan you may receive lower doses. In this case your doctor may prescribe you Tolvaptan tablets with 30 mg or 15 mg Tolvaptan which have to be taken once a day in the morning.

Method of administration

Swallow the tablets without chewing, with a glass of water.

The morning dose is to be taken at least 30 minutes before the morning meal. The second daily dose can be taken with or without food. Avoid drinking grapefruit juice when taking Tolvaptan.

6. It is important to drink plenty of fluids when taking Tolvaptan

Tolvaptan causes water loss because it increases your urine production. This water loss may result in side effects such as dry mouth and thirst or even more severe side effects like kidney problems. It is therefore important that you have access to water and that you are able to drink sufficient amounts when you feel thirsty. Before bed-time you must drink 1 or 2 glasses of water even if you do not feel thirsty and you must also drink water after you urinate at night. Special care must be taken if you have a disease that reduces appropriate fluid intake or if you are at an increased risk of water loss e.g. in case of vomiting or diarrhoea. Due to the increased urine production, it is also important that you always have access to a toilet.

7. If you forget to take Tolvaptan

If you forget to take your medicine you have to take the dose as soon as you remember on the same day. If you do not take your tablet on one day, take your normal dose on the next day. Do not take a double dose to make up for a forgotten dose.

8. If you accidentally take more Tolvaptan than prescribed

If you have taken more tablets than your prescribed dose, drink plenty of water and contact your doctor or your local hospital immediately. Remember to take the medicine pack with you so that it is clear what you have taken. If you take the higher dose very late in the day you may have to go to the toilet at night more frequently.

9. What important side effects of Tolvaptan should I be aware of?

Tolvaptan may cause your liver not to work properly and increase the level of liver enzymes and bilirubin in your blood. To check for any changes in your liver function, your doctor will conduct blood tests:

- before starting treatment with Tolvaptan
- every month for the first 18 months of treatment
- every 3 months thereafter

The following signs indicate that you may have potential liver problems:

- tiredness
- loss of appetite
- right upper abdominal discomfort
- dark urine
- yellowing of skin or eyes (jaundice)
- severe dehydration
- nausea

- vomiting
- fever
- itching of your skin

10. What should I do if I experience any of these signs?

You should inform your doctor immediately if you experience any of the signs mentioned above and seek advice from your doctor. You may need to get additional blood testing.

11. Is it safe to take Tolvaptan while trying to become pregnant, during pregnancy or while breastfeeding?

You should not take Tolvaptan if you are trying to become pregnant or during pregnancy, as it may result in side effects to you and developmental abnormalities in your unborn baby.

Women of childbearing potential must use one effective method of pregnancy prevention for at least 4 weeks before starting therapy, during therapy – even in the case of dose interruptions – and for at least a further 4 weeks after stopping Tolvaptan.

You should discuss with your physician the most suitable form of contraception to use. This is because the use of some contraceptives containing oestrogen may increase the growth and development of cysts in the liver.

You should not breastfeed while taking Tolvaptan.

12. What should I do if I become pregnant or think I may be pregnant while taking Tolvaptan?

You should stop taking Tolvaptan immediately and inform your prescribing doctor immediately so your pregnancy can be monitored.

13. Reporting side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in the package leaflet. Side effects can also be reported to:

SFDA-National Pharmacovigilance and Drug Safety Center

- Email: npc.drug@sfda.gov.sa
- Website: <http://ade.sfda.gov.sa>
- Direct phone: 19999

SPIMACO contact points

If you need additional hard copies of this Guider or report any case of exposure to Tolvaptan during pregnancy, please contact the pharmacovigilance department through the following contact details:

- Email: GPV@spimaco.sa
- Website: <http://spimaco.com.sa/pharmacovigilance/form>
- Hotline: +966 11 252 3393

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