Tolvaptan 15 mg Tablets
Tolvaptan 30 mg Tablets
Tolvaptan 15 mg Tablets + Tolvaptan 45 mg Tablets
Tolvaptan 30 mg Tablets + Tolvaptan 60 mg Tablets
Tolvaptan 30 mg Tablets + Tolvaptan 90 mg Tablets

Package leaflet: Information for the user

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. **What Tolvaptan is and what it is used for**
2. **What you need to know before you take Tolvaptan**
3. **How to take Tolvaptan**
4. **Possible side effects**
5. **How to store Tolvaptan**
6. **Contents of the pack and other information**

1 What Tolvaptan is and what it is used for

Tolvaptan Tablets contains the active substance tolvaptan which blocks the effect of vasopressin, a hormone 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 put pressure on surrounding tissues and reduce 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.

2 What you need to know before you take Tolvaptan

Do not take Tolvaptan:
- if you are allergic to tolvaptan or any of the other ingredients of this medicine (listed in section 6) or if you are allergic to benzazepine or benzazepine derivatives (e.g. benazepril, conivaptan, fenoldopam mesylate or mirtazapine)
- 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 is associated with a very low blood volume (e.g. severe dehydration or bleeding)
- if you have a condition which increases the sodium in your blood
- if you do not realise when you are thirsty
- if you are pregnant
- if you are breast-feeding.

Warnings and precautions
Talk to your doctor before taking Tolvaptan
- if you suffer from liver disease
- if you cannot drink enough water (see "drinking enough water" below) or if you have to restrict your fluid intake
- if you have difficulties urinating (e.g. have an enlarged prostate)
- if you suffer from too high or too low blood sodium
- if you had an allergic reaction in the past to benzazepine, tolvaptan or other benzazepine derivatives (e.g. benazepril, conivaptan, fenoldopam mesylate or mirtazapine), or to any of the other ingredients of this medicine (listed in section 6)
- if you have diabetes
- if you have been told you have high levels of a chemical called uric acid in your blood (which may have caused attacks of gout)
- if you have advanced kidney disease.

This medicine may cause your liver to not work properly. Therefore, please inform your doctor immediately if you have signs that could indicate potential liver problems such as:
- nausea
- vomiting
- fever
- tiredness
- loss of appetite
- pain in the abdomen
- dark urine
- jaundice (yellowing of skin or eyes)
- itching of your skin
- flu-like syndrome (joint and muscle pain with fever).

During treatment with this medicine, your doctor will arrange monthly blood tests to check for changes in your liver function.

Drinking enough water
This medicine 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 (see section 4). 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.

Children and adolescents
Do not give this medicine to children and adolescents (under age of 18 years) because it has not been studied in these age groups.

Other medicines and Tolvaptan
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

The following medicines may increase the effect of Tolvaptan:
- amprenavir, atazanavir, darunavir/ritonavir and fosamprenavir (used to treat HIV/AIDS)
- aprepitant (used to avoid nausea and vomiting in chemotherapy)
- crizotinib and imatinib (used to treat cancer)
- ketoconazole, fluconazole or itraconazole (used to treat fungal infections)
- macrolide antibiotics like erythromycin or clarithromycin
- verapamil (used to treat heart diseases and high blood pressure)
- ciprofloxacin (an antibiotic)
- diltiazem (used to treat high blood pressure and chest pain).

The following medicines may lower the effect of Tolvaptan:
- phenytoin or carbamazepine (used to treat epilepsy)
- rifampicin, rifabutin or rifapentine (used to treat tuberculosis)
- St. John's Wort (a traditional herbal medicinal product for the relief of slightly low mood and mild anxiety).

Tolvaptan may increase the effect of the following medicines:
- digoxin (used to treat irregular heart beat and heart failure)
- dabigatran (used to thin the blood)
- sulfasalazine (used to treat inflammatory bowel disease or rheumatoid arthritis)
- metformin (used to treat diabetes).

Tolvaptan may lower the effect of the following medicines:
- vasopressin analogues such as desmopressin (used to increase blood clotting factors or to control urine output or bedwetting).

These medicines can affect or be affected by Tolvaptan:
- diuretics (used to influence the production of urine). Taken with Tolvaptan these may increase the risk of side effects due to water loss or may cause kidney problems.
- diuretics or other medicines for the treatment of high blood pressure. Taken with Tolvaptan these may increase the risk of low blood pressure when you stand up from sitting or lying down.
- medicines which increase the level of sodium in your blood or which contain large amounts of salt (e.g. tablets that dissolve in water and indigestion remedies). These may increase the effect of Tolvaptan. There is a risk that this may lead to too much sodium in your blood.

It may still be alright for you to take these medicines and Tolvaptan together. Your doctor will be able to decide what is suitable for you.

Tolvaptan with food and drink
Do not drink grapefruit juice when taking this medicine.

Pregnancy and breast-feeding
Do not take this medicine if you are pregnant or breast-feeding.

Women of childbearing age must use reliable contraceptive measures during use of this medicine.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines
Some people may feel dizzy, weak or tired after being given Tolvaptan. If this happens to you, do not drive or use any tools or machines.

Tolvaptan contains lactose and sodium
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3 How to take Tolvaptan

Tolvaptan can only be prescribed by doctors who are specialised in the treatment of ADPKD. Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Dose
The daily amount of Tolvaptan 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.
Tolvaptan 15 mg tablets
Tolvaptan 15 mg tablets + Tolvaptan 45 mg tablets
The 15 mg tablet can be divided into equal doses.
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.

If you take more Tolvaptan than you should
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.

If you forget to take Tolvaptan
If you forget to take your medicine you should take the dose as soon as you remember on the same day. If you do not take your tablets on one day, take your normal dose on the next day. **DO NOT** take a double dose to make up for forgotten individual doses.

If you stop taking Tolvaptan
If you stop taking Tolvaptan your kidney cysts may grow as fast as they did before you started treatment with Tolvaptan. Therefore, you should only stop taking Tolvaptan if you notice side effects requiring urgent medical attention (see section 4) or if your doctor tells you to.

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

4 Possible side effects

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

Serious side effects:

If you notice any of the following side effects, you may need urgent medical attention. Stop taking Tolvaptan and immediately contact a doctor or go to the nearest hospital if you:

- find it difficult to urinate
- experience swelling of the face, lips or tongue, itching, generalised rash, or severe wheezing or breathlessness (symptoms of an allergic reaction).

Tolvaptan may cause your liver not to work properly.
Consult your doctor if symptoms of nausea, vomiting, fever, tiredness, loss of appetite, pain in the abdomen, dark urine, jaundice (yellowing of skin or eyes), itching of your skin or joint and muscle pain with fever occur.

Other side effects:

Very common: may affect more than 1 in 10 people
- thirst (requiring excessive drinking of water)
- headache
- dizziness
- diarrhoea
- dry mouth
- increased need to urinate, to urinate at night, or to urinate more frequently
- fatigue.

Common: may affect up to 1 in 10 people
- dehydration
- high levels of sodium, uric acid and blood sugar
- decreased appetite
- taste changes
- gout
- difficulty sleeping
- fainting
- heart pounding
- shortness of breath
- belly pain
- full or bloated or uncomfortable feeling in the stomach
- constipation
- heartburn
- liver function abnormal
- dry skin
- rash
- itching
- hives
- joint pain
- muscle spasms
- muscle pain
- general weakness
- raised levels of liver enzymes in the blood
- weight loss
- weight gain.

Uncommon: may affect up to 1 in 100 people
- increase of bilirubin (a substance that can cause yellowing of skin or eyes) in the blood.

Not known: frequency cannot be estimated from the available data
- allergic reactions (see above)
- generalised rash
- acute liver failure (ALF).
- increased level of creatine phosphokinase (an enzyme that measures the muscle and heart function) in the blood

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5 How to store Tolvaptan

Keep this medicine out of the sight and reach 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.

This medicinal product does not require any special temperature storage conditions. Store in the original package in order to protect from light.

Do not throw away any 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 Contents of the pack and other information

What Tolvaptan contains
The active substance is tolvaptan.
Each Tolvaptan 15 mg Tablet contains 15 mg tolvaptan.
Each Tolvaptan 30 mg Tablet contains 30 mg tolvaptan.
Each Tolvaptan 45 mg Tablet contains 45 mg tolvaptan.
Each Tolvaptan 60 mg Tablet contains 60 mg tolvaptan.
Each Tolvaptan 90 mg Tablet contains 90 mg tolvaptan.

The other ingredients are lactose monohydrate (see section 2), sodium laurilsulfate, povidone, microcrystalline cellulose, croscarmellose sodium, magnesium stearate.

What Tolvaptan looks like and contents of the pack

The different strengths of Tolvaptan tablets have different shapes and embossing:

15 mg tablet: White to off-white round shaped uncoated tablets with notch, having break-line on both sides and debossed with "A" and "3" on either side of break-line on one side. Diameter of approximately 5.50 mm.

30 mg tablet: White to off-white, round shaped uncoated tablets, debossed with "T5" on one side and plain on the other side, with diameter of approximately 6.80 mm.

45 mg tablet: White to off-white, square shaped uncoated tablets, debossed with "T8" on one side and plain on the other side, with dimensions of approximately 7.70 mm x 7.70 mm.

60 mg tablet: White to off-white, barrel shaped uncoated tablets, debossed with "A0" on one side and plain on the other side, with dimensions of approximately 10.60 mm x 6.30 mm.

90 mg tablet: White to off-white, pentagon shaped uncoated tablets, debossed with "AT" on one side and plain on the other side, with dimensions of approximately 11.27 mm x 11.00 mm.

The following pack sizes are available:
- PVC/Aclar/PVC forming foil and lidding Paper/PET/Aluminum foil.
- PVC/Aclar/PVC forming foil and lidding Aluminum foil.
- OPA/Aluminum/PVC forming foil and lidding Paper/PET/Aluminium foil.

Tolvaptan 15 mg Tablets: blisters with 7 or 28 tablets, and unit dose blisters with 7x1 tablets.

Tolvaptan 30 mg Tablets: blisters with 7 or 28 tablets, and unit dose blisters with 7x1 tablets.

Tolvaptan 15 mg Tablets + Tolvaptan 45 mg Tablets: blisters with 14 (7 tablets of the higher strength + 7 tablets of the lower strength), 28 (14 tablets of the higher strength + 14 tablets of the lower strength) or 56 (28 tablets of the higher strength + 28 tablets of the lower strength) tablets, and unit dose blisters with 56x1 (28x1 tablets of the higher strength + 28x1 tablets of the lower strength) tablets.

Tolvaptan 30 mg Tablets + Tolvaptan 60 mg Tablets: blisters with 14 (7 tablets of the higher strength + 7 tablets of the lower strength), 28 (14 tablets of the higher strength + 14 tablets of the lower strength) or 56 (28 tablets of the higher strength + 28 tablets of the lower strength) tablets, and unit dose blisters with 56x1 (28x1 tablets of the higher strength + 28x1 tablets of the lower strength) tablets.

Tolvaptan 30 mg Tablets + Tolvaptan 90 mg Tablets: blisters with 14 (7 tablets of the higher strength + 7 tablets of the lower strength), 28 (14 tablets of the higher strength + 14 tablets of the lower strength) or 56 (28 tablets of the higher strength + 28 tablets of the lower strength) tablets, and unit dose blisters with 56x1 (28x1 tablets of the higher strength + 28x1 tablets of the lower strength) tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

TEVA UK Limited, Ridings Point, Whistler Drive, Castleford, WF10 5HX, United Kingdom

Manufacturer

Teva Operations Poland Sp. z.o.o, ul. Mogilska 80, Kraków, 31-546, Poland

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