

Tolvaptan

Frequently Asked Questions (for patients)

1. What is tolvaptan?

Tolvaptan is a medication that slows the growth of kidney cysts in patients with autosomal dominant polycystic kidney disease, also known as ADPKD. This may slow the progress of kidney problems in some patients.

Compared to those who did not take tolvaptan, those who took it had:

- Less growth in total kidney volume (TKV) each year
- Fewer episodes of pain in the kidneys
- Slower decline in kidney function

2. How does tolvaptan work?

Tolvaptan blocks a hormone called vasopressin. Vasopressin helps the body hold onto water. Vasopressin is also one of many factors that lead to growth of kidney cysts in patients with ADPKD. Blocking this hormone may help to slow cyst growth.

Another study called REPRISÉ lasted 1 year and included 1,370 patients who had lower levels of kidney function compared to the patients in TEMPO 3:4, as well as some patients who were older than those in TEMPO 3:4. There were two groups of patients studied:

3. Has tolvaptan been studied?

Health Canada has approved tolvaptan for use in patients with ADPKD based on studies that have been completed.

- 18 to 55 years old with an eGFR of 25 to 65 mL/min/1.73 m²
- 56 to 65 years old with an eGFR of 25 to 44 mL/min/1.73 m² that was decreasing by more than 2 mL/min/1.73 m² every year

The largest study was called TEMPO 3:4. This study lasted 3 years and included 1,445 patients aged 18 to 50 with early stage ADPKD. All of the people in the study had large kidneys (a total kidney volume greater than 750 mL), but still had good kidney function (an average eGFR* of 80 mL/min/1.73 m²).

Like the results from the TEMPO 3:4 study, the REPRISÉ study found that kidney function (eGFR) decreased by about 1 mL/min/1.73 m² less every year in patients who took tolvaptan, compared to those who did not.

Not all patients could tolerate tolvaptan. Side effects reported in both studies

included:

- Feeling too thirsty
- Problems with passing too much urine
- Signs of a liver problem (measured in blood tests)

4. Will tolvaptan reduce or delay the need for dialysis or a kidney transplant?

Currently, it has not been proven that tolvaptan reduces or delays the need for dialysis or kidney transplant, because the studies completed to date did not last long enough to answer this question.

However, the results of the TEMPO 3:4 and REPRIZE studies are promising because they showed that kidney function decreased slower over 1 to 3 years in patients who took tolvaptan, compared to those who did not. The hope is that tolvaptan will continue to slow the progress of kidney problems over the long term.

5. Is tolvaptan a good medication for me?

Tolvaptan is not for everyone with ADPKD. Talk to your kidney doctor to decide if tolvaptan is a good fit for you. Based on what we know from studies to date, kidney doctors and pharmacists at BC Renal believe that the patients most likely to benefit from tolvaptan are people between the ages of 18 and 65 who:

- Are experiencing rapid progression of their kidney disease due to ADPKD

- Have rapidly growing kidneys or declining kidney function

The decision to use tolvaptan is based on each patient's medical history, status, and medications. Since side effects exist, it is important to balance the risks and the benefits. In some people, it may be decided not to start tolvaptan because of its side effects.

Patients taking tolvaptan need to have frequent blood tests done to check for signs of a liver problem. If you are unable to complete the regular blood work requirements, the pharmacy will not be able to dispense tolvaptan to you.

6. What side effects could occur from taking tolvaptan and how do I minimize them?

The expected side effects from taking tolvaptan are:

- Increased thirst
- Passing more urine during the day and night

Making adjustments to your diet can help decrease your thirst and the amount of urine you pass. These can include limiting salt and protein intake. Speak to your kidney doctor or kidney dietitian for more information on this.

Drink plenty of water to avoid becoming extremely thirsty or dehydrated (dry). If you have an illness that causes you to vomit or have diarrhea AND you are unable to

eat or drink normally, stop taking tolvaptan until you are able to drink fluids again. Contact your doctor if you have to stop taking tolvaptan for 2 days.

Serious side effects that occur less often include:

- **A heartbeat that does not feel normal, muscle weakness and a general feeling of being unwell:** these are signs of increased levels of potassium in the blood.
- **Joint pain (commonly in the big toe), followed by redness, swelling or warmth:** these are signs of increased levels of uric acid in the blood, resulting in a condition called gout
- **Yellowing of the skin or eyes, dark urine, upset stomach, throwing up, or not being hungry:** these are signs of a liver problem.

Patients who take tolvaptan are monitored closely by their kidney doctors. They are required to do blood tests and have regular follow-up.

7. What can I do to ensure tolvaptan is safe for me?

Talk to your kidney doctor. If you choose to take tolvaptan, you will be asked to sign an agreement. The agreement will state that you understand the risks of developing liver problems and agree to do blood tests to check liver function at the following times:

- Monthly for the first 18 months
- Every 3 months for the following year
- Every 3 to 6 months thereafter

These blood tests are necessary to prevent serious liver damage. If you do not complete the blood tests, the pharmacy cannot dispense tolvaptan to you.

Lastly, some foods and other medications (prescription, over-the-counter or supplements) may interact with tolvaptan.

For example, avoid drinking grapefruit juice because it can cause tolvaptan levels to increase in the body. Talk with your kidney doctor and pharmacist before starting any new medication so that they can ensure that it is safe for you.

**eGFR or the estimated glomerular filtration rate is a blood test used to measure kidney function.*