Key Takeaways for Clinicians from the KDIGO 2025 Clinical Practice Guideline for the Evaluation, Management, and Treatment of ADPKD: Therapies to delay the progression of kidney disease

1 Basic actions to delay disease progression

Patients with ADPKD should be encouraged to follow 4 basic actions to delay disease progression: maintain optimal blood pressure and body weight, follow a low-salt diet, and maintain a high-water intake. Evidence from observational studies and clinical trials strongly suggests that achieving these goals delays disease progression and extends the survival of the kidneys and people with ADPKD.

2 Vasopressin receptor antagonist (tolvaptan)

Tolvaptan is recommended in adults with ADPKD and eGFR ≥25 ml/min/1.73 m² at risk of rapidly progressive disease and who have no absolute contraindications (i.e., planning pregnancy/pregnant/breast-feeding; impaired ability to manage aquaretic side effects; urinary tract obstruction; requirement for strong CYP3A inhibitors; significant liver disease other than polycystic liver disease; Figure 1). Potential benefits, harms, and uncertainties regarding long-term treatment with tolvaptan should be discussed.

3 Methods to evaluate rapid disease progression for tolvaptan

The Mayo Imaging Classification (MIC) is recommended to assess rapid progression when imaging is available to measure kidney volumes with subclass 1C to 1E as a criterion for starting tolvaptan (Figure 1). Yearly decline of eGFR ≥3 ml/min/1.73 m² over the previous 3–5 years where there are no other reasons for the decline or a PROPKD score >6 are alternative methods.

4 Management of aquaretic side effects of tolvaptan

Patients starting tolvaptan should be informed that it causes an immediate increase in urine output that requires a matched water intake to avoid dehydration. To improve tolerability, tolvaptan is started at a low dose and titrated upwards (Figure 2); however, the dose can be down-titrated if necessary. Patients should be assured that with time, polyuria decreases to some extent, and the high urine output becomes more accustomed and tolerated. Patients should be counselled to hold tolvaptan when access to water or ability to drink is limited because of travelling or illness, or in situations when large extrarenal losses of water are present, such as episodes of gastroenteritis or in very hot weather.

5 Management of elevations in liver enzymes due to tolvaptan

Liver enzyme elevations occur in approximately 5% of patients within the first 18 months of treatment. To avoid the risk of severe liver injury, all patients should have liver function tests at baseline, monthly for first 18 months, every 3 months thereafter (Figure 3). Tolvaptan should be held immediately when elevations in enzymes occur and discontinued permanently if the elevations reach 3 or more times the upper limit of normal in the absence of other explanations.

6 Other potential adverse events of tolvaptan

Patients should also be informed that tolvaptan causes a rapid but slight increase in serum creatinine which is reversible when the drug is discontinued. Other rare and relatively minor risks of tolvaptan treatment include flares of gout and myalgias with elevations of creatine kinase. All people with ADPKD should have a "sick day plan" that includes skipping doses where there is a transient risk of volume depletion.

7 Increased water intake in the absence of tolvaptan

Increased water intake suppresses vasopressin release and is therefore recommended in all patients with an eGFR ≥25 ml/min/1.73 m². Patients should be provided individualized counseling to drink 2–3 liters of water per day unless there is a contraindication such as a medical condition or a medication interfering with the capacity to dilute urine. Increased water intake is not an alternative to tolvaptan in patients with rapid disease progression.

8 Other therapies

Other therapies (mTOR inhibitors, metformin, statins, somatostatin analogs, SGLT2i, ketogenic interventions, complementary) have not been proven to slow the decline in kidney function in ADPKD, and should not be used for this purpose unless further evidence becomes available.

Figure 1

Initiation of tolvaptan should be offered to adults with ADPKD and:
eGFR ≥25 ml/min per 1.73 m²

AND

Risk of rapid disease progression as indicated by either:
Mayo class 1C to 1E
OR
Historical rate of eGFR decline (≥3 ml/min per 1.73 m² per year)

Figure 2

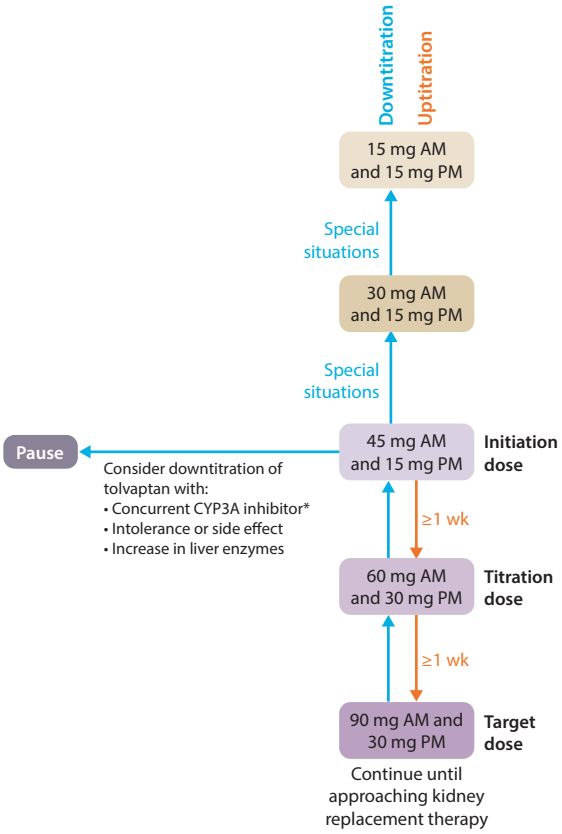
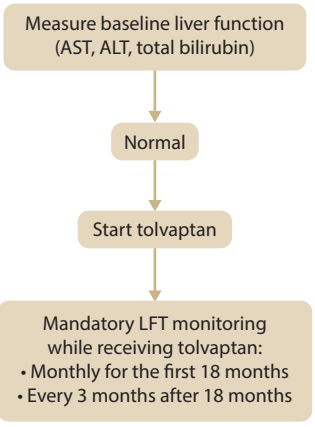


Figure 3



ADPKD, autosomal dominant polycystic kidney disease; CYP3A, cytochrome P450, 3A inhibitors; eGFR, estimated glomerular filtration rate; LFT, liver function tests; mTOR, mammalian target of rapamycin; PROPKD, Predicting Renal Outcomes in Polycystic Kidney Disease; SGLT2i, sodium-glucose cotransporter-2 inhibitors