Prokitav® (tolvaptan)
Prokitav 45 mg and 15 mg Tablets
Prokitav 60 mg and 30 mg Tablets
Prokitav 90 mg and 30 mg Tablets

Prokitav® (tolvaptan) Healthcare Professional (HCP) prescribing checklist for treatment initiation – section A

This (HCP) prescribing checklist contains important safety information that a patient needs to be aware of before and during the treatment with Prokitav to ensure the safe and effective use of the product.

Patient's name		Patient's hospital number	

Prokitav (tolvaptan) is indicated to slow the progression of cyst development and renal insufficiency of autosomal dominant polycystic kidney disease (ADPKD) in adults with chronic kidney disease (CKD) stage 1 to 4 at initiation of treatment with evidence of rapidly progressing disease. The following checklists are provided to help you assess patient suitability for Prokitav treatment prior to initiation (Section A) and during treatment (Section B). For full information on Prokitav, please consult the Summary of Product Characteristics (SPC). If you require further information on Prokitav, please contact Hikma Medical Information at SAMA@hikma.com.

Section A: Checklist for patient assessment prior to initiation of Prokitav treatment

CONTRAINDICATIONS – If any of the following apply to the patient, Prokitav use is contraindicated	Yes	No
Elevated liver enzymes and/or signs or symptoms of liver injury prior to initiation of treatment that meet the requirements for permanent discontinuation of Prokitav. Recommendations for permanent discontinuation include: • Alanine or aspartate aminotransferases (ALT or AST) > 8-times upper limit of normal (ULN) • ALT or AST > 5-times ULN for more than 2 weeks • ALT or AST > 3-times ULN and (bilirubin total (BT) > 2-times ULN or International Normalized Ratio (INR) > 1.5) • ALT or AST > 3-times ULN with persistent symptoms of hepatic injury (fatigue, anorexia, nausea, right upper abdominal discomfort, vomiting, fever, rash, pruritus, dark urine or jaundice)		
Hypersensitivity to the active substance or to any of its excipients, or to benzazepine or benzazepine derivatives		
Volume depletion		
Hypernatraemia		
Anuria		
Inability to perceive or respond to thirst		
Pregnancy		
Breastfeeding		
WARNINGS AND PRECAUTIONARY CONDITIONS – Please refer to the SPC for information on appropriate tests and monitoring required	Yes	No
Raised liver enzymes, AST and/or ALT stabilised at no greater than 3-times ULN **In case of abnormal baseline levels below the limits for permanent discontinuation, treatment can only be initiated if the potential benefits of treatment outweigh the potential risks and liver function testing must continue at increased time frequency. The advice of a hepatologist is recommended.**		
Severe hepatic impairment (Child-Pugh class C) (benefit vs. risk must be evaluated carefully)		
Limited access to water		
Dehydration		
Urinary outflow obstruction (e.g. prostatic hypertrophy)		
Fluid and electrolyte imbalance		
Serum sodium abnormalities		
Anaphylaxis		
Lactose intolerance		
Diabetes mellitus		
Uric acid increases		
CKD late stage 4 (eGFR< 25 mL/min/1.73 m^2) and stage 5		
Effect of Prokitav on glomerular filtration rate (GFR): a reversible reduction in GFR has been observed in ADPKD trials at initiation of Prokitav treatment		
Medicines likely to interact with Prokitav are CYP3A inhibitors, CYP3A inducers, CYP3A substrates, transporter substrates, diuretics, medicinal products that increase serum sodium concentration, diuretics or non-diuretic anti-hypertensive medicines and vasopressin analogues. Prokitav dose must be reduced in patients taking drugs that are moderate or strong CYP3A inhibitors, as concomitant use of these drugs increases Prokitav exposure. See Prokitav SPC, Sections 4.2 and 4.5 for the complete information).		

PRESCRIBING DECISION (initiation)

Based on the satisfactory test results, I intend to initiate treatment with Prokitav at the following dose (enter dosing):

Clinician's name		Date	

If you have decided to prescribe Prokitav, the patient has to be informed of the following points:

- There is a need for monthly blood tests for liver function during the first 18 months of therapy and every 3 months thereafter
- The patient must be vigilant for signs and symptoms of hepatic injury
- The patient must have access to water, be able to drink sufficient amounts, and to drink 1-2 glasses before bedtime and with each episode of nocturia. The patient must be vigilant for signs and symptoms of dehydration

- Additional tests and monitoring will be performed as required
- A female of childbearing potential must use adequate contraceptive measures for at least 4 weeks before starting therapy, during use and for at least a further 4 weeks after stopping Prokitav. If pregnancy occurs, they must inform the prescribing doctor immediately
- Advise patients to read the Patient Information Leaflet and provide them with a patient/carer education brochure and a patient alert card

Any suspected adverse reactions to Prokitav should be reported to Jazeera Pharmaceutical Industries at the following email address: SAPV@hikma.com and/or to Saudi Food and Drug Administration (SFDA) at the following contact details:

E-mail: npc.drug@sfda.com,

Website: https://ade.sfda.gov.sa,

Call center number: 19999, or QR Code:

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Prokitav® (tolvaptan) Healthcare Professional (HCP) prescribing checklist for treatment initiation – section B

This (HCP) prescribing checklist contains important safety information that a patient needs to be aware of before and during the treatment with Prokitav to ensure the safe and effective use of the product.

Patient's name		Patient's hospital number	

Prokitav (tolvaptan) is indicated to slow the progression of cyst development and renal insufficiency of autosomal dominant polycystic kidney disease (ADPKD) in adults with chronic kidney disease (CKD) stage 1 to 4 at initiation of treatment with evidence of rapidly progressing disease. The following checklists are provided to help you assess patient suitability for tolvaptan treatment prior to initiation (Section A) and during treatment (Section B). For full information on tolvaptan, please consult the Summary of Product Characteristics (SPC). If you require further information on tolvaptan, please contact Hikma Medical Information at SAMA@hikma.com.

Section B: Checklist for patient assessment for ongoing eligibility for tolvaptan treatment

The following checklist should be completed monthly for the first 18 months of tolvaptan treatment and then every 3 months thereafter.

All adverse events should be reported to the SFDA and JPI as described in the box below.

HEPATIC INJURY	Yes	No
Is the patient showing any signs or symptoms of liver injury? (fatigue, anorexia, nausea, right upper abdominal discomfort, vomiting, fever, rash, pruritus, dark urine or jaundice). **If the answer is Yes, treatment with tolvaptan must be immediately interrupted, the cause investigated and the occurrence reported.**		

Liver function test results	**Recommended action**
Clinically significant abnormal ALT or AST increases	**Immediately interrupt tolvaptan treatment, investigate the cause of the raised liver enzyme(s) and repeat tests including ALT, AST, BT and alkaline phosphatase (AP) as soon as possible (ideally within 48–72 hours). Report decision to JPI using the reporting mechanism below. Testing must continue at increased time frequency until symptoms/signs/laboratory abnormalities stabilize or resolve.**
Liver function results stabilize if ALT and AST levels remain below 3-times ULN	**Restart tolvaptan treatment cautiously at same or lower dose with frequent monitoring and report decision to JPI using the reporting mechanism below.**
ALT or AST > 8-times ULN	**Permanently discontinue treatment and report decision to JPI using the reporting mechanism below.**
ALT or AST > 5-times ULN for more than 2 weeks	
ALT or AST > 3-times ULN and (BT > 2-times ULN or International Normalized Ratio (INR) >1.5)	
ALT or AST > 3-times ULN with persistent symptoms of hepatic injury (noted above)	

PRESCRIBING DECISION (ongoing treatment) – Titrate dose upward, if tolerated, with at least weekly intervals between up-titrations	Tick box
Based on tolerability, monitoring and other tests performed on this patient (select one option below)	
I intend to continue tolvaptan at the following dose (enter dose)	
I have decided to interrupt treatment with tolvaptan	
I have decided to permanently discontinue treatment with tolvaptan	

Clinician's name		Date	

If you have decided to continue to prescribe tolvaptan, the patient has to be informed of the following points:

- There is a need for monthly blood tests for liver function during the first 18 months of therapy and every 3 months thereafter
- The patient must be vigilant for signs and symptoms of hepatic injury
- The patient must have access to water, be able to drink sufficient amounts and to drink 1-2 glasses before bedtime and with each episode of nocturia. The patient must be vigilant for signs and symptoms of dehydration
- Additional tests and monitoring will be performed as required
- A female of childbearing potential must use adequate contraceptive measures for at least 4 weeks before starting therapy, during use and for at least a further 4 weeks after stopping tolvaptan. If pregnancy occurs, they must inform the prescribing doctor immediately

- Remind the patient that they can refer to the Patient Information Leaflet and patient/carer education brochure for more information, and to always carry the patient alert card with them.

Any suspected adverse reactions to tolvaptan should be reported to Jazeer Pharmaceutical Industries at the following email address: SAPV@hikma.com and/or to Saudi Food and Drug Administration (SFDA) at the following contact details:

E-mail: npc.drug@sfda.com,

Website: https://ade.sfda.gov.sa,

Call center number: 19999, or QR Code:

This document is approved by The Executive Directorate of Pharmacovigilance, at SFDA.