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LUPIN GROUP COMPANY

Pharmacist Booklet

TOLVAPTAN LUPIN

(tolvaptan tablets)

Contents

About this guide

This guide contains important information about ordering Tolvaptan Lupin supply for your patients.

Under the risk management plan mandated by the TGA, Generic Health Pty Ltd has prepared this guide to facilitate safe and effective use of Tolvaptan Lupin.

For more information on Tolvaptan Lupin, please visit our website **www.generichealth.com.au/tolvaptan/pharmacists** or contact our team at:

Email: **customer.service@generichealth.com.au**

Phone: 03 9809 7900, Option 1

Note: This guide is designed to be used in conjunction with the full Product Information and is not a substitute for the Product Information. It is not intended to replace professional or clinical judgment.

This guide is only intended for Healthcare Professionals only when dispensing Tolvaptan Lupin for autosomal dominant polycystic kidney disease (ADPKD).

Important Information About Tolvaptan Lupin

WARNING: Tolvaptan has been associated with idiosyncratic elevations of blood alanine and aspartate aminotransferases (ALT and AST), rarely associated with concomitant elevations in bilirubin-total (BT). To help mitigate the risk of liver injury, blood testing for hepatic transaminases is required prior to initiation of Tolvaptan Lupin, then continually monthly for 18 months, then every 3 months thereafter during treatment with Tolvaptan Lupin (see Section 4.4 Special Warnings and Precautions for Use in the full Product Information). Prescriber education and certification on the risk of liver injury and the importance of regular liver function monitoring is mandatory. These are available through the Tolvaptan portal on the Generic Health website.

Prior to initiation of Tolvaptan Lupin, blood testing for hepatic transaminases (ALT and AST) and bilirubin (BT) is required to mitigate the risk of significant and/or irreversible liver injury. Blood levels of liver enzyme and bilirubin should be monitored every month for 18 months and at regular 3-monthly intervals thereafter.

Prescriber education and certification on the risk of liver injury and the importance of regular liver function monitoring is compulsory. Pharmacists should only dispense Tolvaptan Lupin prescribed by certified nephrologists. Prescriber's certification status can be verified at **www.tolvaptanlupinverify.com**

Total Daily Dose Options

60 mg
(45 mg + 15 mg combination pack)

OR

90 mg
(60 mg + 30 mg combination pack)

OR

120 mg
(90 mg + 30 mg combination pack)

Tolvaptan Lupin Order Process

Initial Tolvaptan Lupin Order Verify prescriber's certification status at **www.tolvaptanlupinverify.com**	• Nephrologist provides patient with approved PBS authority script (or private script) for Tolvaptan Lupin. • Patient takes script to their nominated pharmacy. • Pharmacist verifies that the prescriber is certified by cross checking the Tolvaptan Lupin prescriber database. • If a prescriber is not certified the pharmacist should: **1.** Contact the non-certified prescriber to remind them of the TGA requirements for Tolvaptan Lupin and check whether Tolvaptan Lupin should still be dispensed to the patient. **2.** Contact Generic Health Medical Information team on 03 9809 7900, Option 2. Generic Health will then contact the prescriber for education and certification. • Contact your preferred wholesaler to order Tolvaptan Lupin. • The initial Tolvaptan Lupin order must only be given for 28 days of treatment per patient. • Pharmacist should notify the patient when their Tolvaptan Lupin has arrived at the pharmacy.
Subsequent Tolvaptan Lupin Orders	• Patients must have their liver function monitored at regular intervals to continue receiving Tolvaptan Lupin. • Prescribers are responsible for checking that patients have had a valid liver function test (LFT) and are eligible to continue treatment. • Pharmacists are advised to use the same wholesaler each time Tolvaptan Lupin is ordered as it is a specialty product which may not be routinely stocked. • Prescribers will advise patients if changes to their prescription are needed. Patients must provide a new prescription if their dose changes. • Pharmacist places their next Tolvaptan Lupin order through their preferred wholesaler. • Patients are advised to use the same pharmacy each time Tolvaptan Lupin is dispensed to ensure that there are no issues with continuity of supply. • Subsequent orders must only be given for 28 days of treatment per patient.
Dose Adjustments	• Dose adjustments can be made at the discretion of the prescriber. • Patients must receive a new prescription for dose adjustments.
Treatment Discontinuation	• Patients can discontinue therapy at any time or have a temporary break in treatment at the discretion of the prescriber.

About Tolvaptan Lupin

Australian Approved (generic) Name	Tolvaptan
Trade/Brand Name	Tolvaptan Lupin
Pharmaceutical Form	Tablets
Dosage	Twice daily split dose of: 45 mg + 15 mg; **OR** 60 mg + 30 mg; **OR** 90 mg + 30 mg
Strength(s)	15 mg, 30 mg, 45 mg, 60 mg or 90 mg
Supplier/Sponsor	Generic Health Pty Ltd
Pack Size	• Combination pack of 45 mg + 15 mg tablets – supplied in a blister pack of 56 tablets • Combination pack of 60 mg + 30 mg tablets – supplied in a blister pack of 56 tablets • Combination pack of 90 mg + 30 mg tablets - supplied in a blister pack of 56 tablets

Pharmacological Class and Action	**Pharmacological Class:** Vasopressin antagonist **Mechanism of Action:** Specifically blocks the binding of arginine vasopressin (AVP) at the V2 receptors of the distal portions of the nephron.
Indication	Tolvaptan Lupin 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 3 at initiation of treatment with evidence of rapidly progressing disease.
PBS Criteria – Initial Treatment	**PBS Treatment Criteria** Must be treated by a nephrologist. **PBS Clinical Criteria** • Adult ADPKD patient. • Patient must have an eGFR between 30 mL/min/1.73m^2 and 89 mL/min/1.73m^2 at the initiation of treatment with tolvaptan for this condition. **AND** • Patient must have or have had rapidly progressing disease at the time of initiation of tolvaptan for this condition. Rapidly progressing disease is defined as either of the following: – A decline in eGFR ≥5 mL/min/1.73m^2 within one year. **OR** – An average decline in eGFR of ≥2.5 mL/min/1.73m^2 per year over a period of 5 years.
PBS Criteria – Continuing Treatment	**PBS Treatment Criteria** • Must be treated by a nephrologist or in consultation with a nephrologist. **PBS Clinical Criteria** • Adult ADPKD patient. • Patient must have previously received PBS-subsidised treatment with tolvaptan for this condition. **AND** • Patient must not have end-stage renal disease, defined as an eGFR of <15 mL/min/1.73m^2. **AND** • Patient must not have had a kidney transplant.

Tolvaptan Lupin Dosing

Tolvaptan Lupin is to be administered twice daily in split dose regimens, with a:

- higher dose to be taken in the morning, ie. at least 30 minutes before breakfast or the morning meal; and
- second, lower dose taken 8 hours later (with or without food).

Tolvaptan Lupin should not be taken with grapefruit juice due to increase in peak tolvaptan concentration.

Dose Titration Process

	Initial Dose	→ At least 1 week after initial dose (if tolerated)	First Titration	→ At least 1 week after first titration (if tolerated)	Second Titration
Morning Dose (at least 30 minutes before meal)	45 mg		60 mg		90 mg
Second Dose (8 hours later with or without food)	15 mg		30 mg		30 mg
Total Daily Dose	**60 mg**		**90 mg**		**120 mg**

Dose titration has to be performed cautiously to ensure that high doses are not poorly tolerated through overly rapid up-titration:

- Patients may be down-titrated to lower doses based on tolerability.
- Patients should be maintained on the highest tolerable tolvaptan dose.

Dose Adjustments

Dose Adjustments for Patients Taking Strong CYP3A Inhibitors

Tolvaptan Lupin Daily Split Dose	Reduced Dose Once Daily
90 mg + 30 mg	30 mg (further reduction to 15 mg if 30 mg are not well tolerated)
60 mg + 30 mg	30 mg (further reduction to 15 mg if 30 mg are not well tolerated)
45 mg + 15 mg	15 mg

Dose Adjustments for Patients Taking Moderate CYP3A Inhibitors

Tolvaptan Lupin Daily Split Dose	Reduced Split Dose
90 mg + 30 mg	45 mg + 15 mg
60 mg + 30 mg	30 mg + 15 mg
45 mg + 15 mg	15 mg + 15 mg

Note: Further reductions have to be considered if patients cannot tolerate the Tolvaptan Lupin reduced doses.

Storage

Store below 25°C.

Protect from light and moisture.

More Information

Tolvaptan Lupin is distributed in Australia by Generic Health Pty Ltd.

For more information on Tolvaptan Lupin, please contact:

Email: **customer.service@generichealth.com.au**

Phone: **03 9809 7900**, Option 1

Website: **www.generichealth.com.au**

For adverse event reporting or medical information, please contact:

Email: **ghinfo@generichealth.com.au**

Phone: **03 9809 7900**, Option 2

Website: **www.generichealth.com.au**

Adverse events should be reported within 24 hours of awareness or on the next working day.

PBS Information: Authority required

Refer to full PBS schedule for full authority information.

PLEASE REVIEW THE FULL PRODUCT INFORMATION (PI) BEFORE PRESCRIBING.

The approved PI is available from Generic Health Pty Ltd by calling 03 9809 7900 or on the website at www.generichealth.com.au/tolvaptan/pharmacists

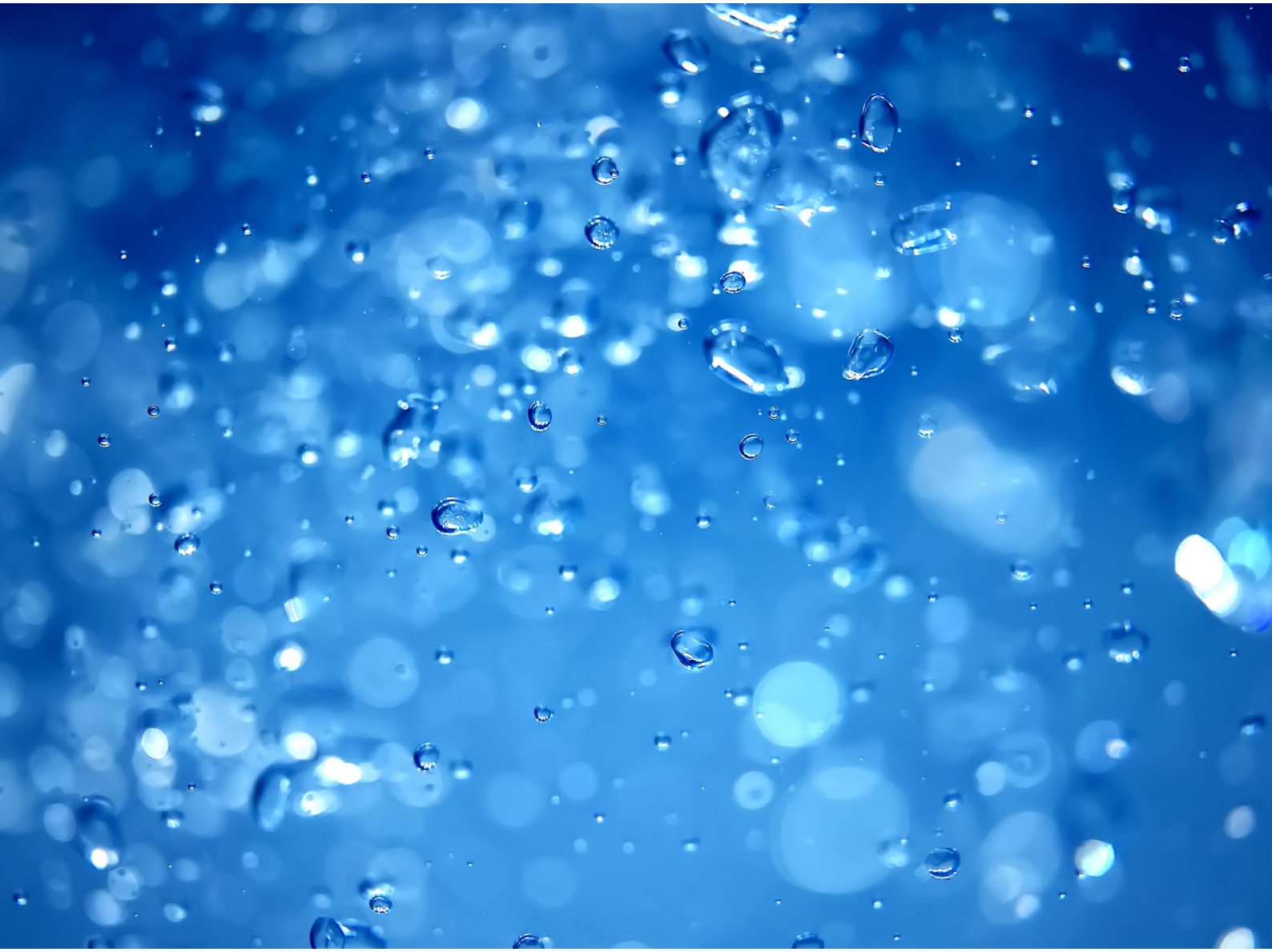
Tolvaptan Lupin (tolvaptan tablets) minimum Product Information (PI).

Tolvaptan has been associated with idiosyncratic elevation of blood alanine and aspartate aminotransferases, rarely associated with concomitant elevations in total bilirubin. To help mitigate the risk of liver injury, blood testing for hepatic transaminases is required prior to initiation of Tolvaptan Lupin, then continually for 18 months, then every 3 months thereafter during treatment with Tolvaptan Lupin. Prescriber education and certification on the risk of liver injury and the importance of regular liver function monitoring is mandatory. (see PI for full details).

INDICATION: Tolvaptan Lupin are 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 3 at initiation of treatment with evidence of rapidly progressing disease. **CONTRAINDICATIONS:** Hypersensitivity to the active substance, benzazepine derivatives or to any of the excipients; elevated liver enzymes and/or signs or symptoms of liver injury prior to initiation of treatment that meet the requirements for permanent discontinuation of tolvaptan; volume depletion; anuria; hypernatremia; inability to perceive or respond to thirst. ***Pregnancy:*** Tolvaptan Lupin must not be used during pregnancy (Category D). ***Lactation:*** Tolvaptan Lupin are contraindicated during breastfeeding. **PRECAUTIONS:** Liver injury or disease: tolvaptan can cause irreversible and potentially fatal liver injury; the prescribing physicians must comply fully with the safety measures outlined in the PI. Potent aquaresis may induce hypernatremia, hyperkalemia or other electrolyte imbalances. Dehydration and hypovolaemia: patients receiving Tolvaptan Lupin should have access to water and should continue ingestion of fluid in response to thirst. ***Diabetes:*** Tolvaptan may cause hyperglycaemia, lactose and galactose intolerance, urinary outflow obstruction. Ability to drive and use machines may be impaired. Paediatric use is not recommended. **INTERACTIONS:** CYP3A inhibitors, CYP3A inducers, digoxin, P-glycoprotein inhibitors (eg. ciclosporin, quinidine), vasopressin analogues (eg. desmopressin), diuretics and medicinal products that increase serum sodium concentration. Co-administration with grapefruit juice should be avoided. **ADVERSE EFFECTS:** Very common adverse effects include thirst, polyuria, nocturia, pollakiuria and polydipsia. Common adverse effects include palpitations, constipation, dyspepsia, blood uric acid increased, decreased appetite, gout, hypernatraemia, hyperuricaemia, dry skin, eczema, rash, diarrhoea, alanine aminotransferase increased and hepatic enzyme increased. For further information about very common and common adverse effects, please see the full PI. **DOSAGE AND ADMINISTRATION**: Tolvaptan Lupin is to be administered twice daily in split dose regimens, initiated at 45 mg (morning dose) + 15 mg (evening dose). 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. The dose is to be titrated upward to a split-dose regimen of 90 mg tolvaptan (60 mg + 30 mg) per day and then to a target split-dose regimen of 120 mg tolvaptan (90 mg + 30 mg) per day, with at least weekly intervals between titrations. The maximum tolerated dose should be maintained. For oral use, tablets must be swallowed without chewing and with a glass of water.

Date of preparation of minimum PI: December 2024

Notes



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