Tolvaptan (tol-vap-tan)

**Summary**

**Indications**
Treatment of significant hypervolemic and euvolemic hyponatremia (serum sodium <125 mEq/L or less marked symptomatic hyponatremia that has resisted correction by fluid restriction), including patients with heart failure and Syndrome of Inappropriate Antidiuretic Hormone (SIADH).

**Classification**
Therapeutic: electrolyte modifiers
Pharmacologic: vasopressin antagonists

**Pregnancy Category**
C

**Pharmacology**

- **Absorption:** 40% absorbed following oral administration.
- **Distribution:** 99%.
- **Metabolism and Excretion:** Extensively metabolized primarily by the CYP3A4 enzyme system; no renal elimination.
- **Half-life:** 12 hr.

**TIME/ACTION PROFILE**

<table>
<thead>
<tr>
<th>ROUTE</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO</td>
<td>within 8 hr</td>
<td>2–4 hr†</td>
<td>7 days</td>
</tr>
</tbody>
</table>

† Blood level

**Contraindications/Precautions**

- Contraindicated in: Urgent need to acutely raise serum sodium; Patients who cannot appropriately sense/respond to thirst; Hypovolemic hyponatremia; Concurrent use of strong or moderate CYP3A inhibitors; Anuria; Liver disease; Lactation: Avoid use.

Use Cautiously in: Severe malnutrition, alcoholism or advanced liver disease (↑ risk of osmotic demyelination, correct electrolyte abnormalities at a slower rate); Geront: May have ↓ sensitivity to effects; GI: Use only if the potential benefit justifies the potential risks to the fetus. Pediatric safety and effectiveness not established.

**Adverse Reactions/Side Effects**

- **CNS:** weakness
- **GI:** hepatotoxicity, constipation, dry mouth
- **GU:** polyuria
- **F and E:** thirst
- **Metab:** hyperglycemia
- **Neuro:** osmotic demyelination

**Interactions**

- **Drug-Drug:** Strong inhibitors of the CYP3A enzyme system including ketoconazole, clarithromycin, itraconazole, saquinavir, ritonavir, and nefazodone may affect levels and may ↑ effects and risk of toxicity; concurrent use should be avoided. Moderate CYP 3A inhibitors including erythromycin, fluconazole, aprepitant, diltiazem, and verapamil may have a similar effect and should also be avoided. Inducers of the CYP3A enzyme system including rifampin may affect levels and effectiveness; dosage adjustments may be necessary. Levels and risk of toxicity are also ↑ by P gp inhibitors including cyclosporine; dosage adjustments may be necessary. May ↓ digoxin levels, monitor carefully. May ↑ risk of hypocalcemia with angiotensin receptor blockers, ACR inhibitors, and potassium-sparing diuretics.

- **Drug-Food:** Grapefruit juice may affect levels and the risk of toxicity; avoid concurrent use.

**Route/Dosage**

- **PO (Adults):** 15 mg once daily initially; may be ↑ at intervals of at least one day to 30 mg once daily, up to a maximum of 60 mg once daily. Do not use for longer than 30 days.

**Nursing Implications**

- Monitor neurologic status and assess for signs and symptoms of osmotic demyelination syndrome (inability to concentrate urine, obtundation, motor or sensory change, ataxia, nystagmus, muscle weakness, confusion, ataxia, altered mental status). If a rapid ↑ in sodium or symptoms occur, discontinue the drug and consider administration of hypotonic fluid.
Monitor fluid balance. If hypovolemia occurs interrupt or discontinue tolvaptan and provide supportive care (monitor vital signs, balance fluid and electrolytes).

Monitor for signs and symptoms of liver injury (fatigue, anorexia, right upper abdominal discomfort, dark urine, jaundice) periodically during therapy. If symptoms occur, discontinue therapy.

Lab Test Considerations: Monitor serum sodium levels frequently during initiation and dose titration and periodically during therapy. Too rapid correction of hyponatremia (> 12 mEq/L/24 hr) can cause osmotic demyelination syndrome.

Monitor serum potassium in patients with serum potassium > 5 mEq/L or taking medication known to increase potassium.

Potential Nursing Diagnoses
- Risk for imbalanced fluid volume

Implementation
- Initiate and re-initiate therapy in a hospital.
- Avoid fluid restriction during first 24 hr of therapy.
- PO: Administer once daily without regard to meals.

Patient/Family Teaching
- Instruct patient to take tolvaptan as directed. Avoid drinking grapefruit juice during therapy; may cause ↑ levels. Take missed doses as soon as remembered, but avoid taking extra dose. Do not double doses. Do not stop and restart therapy. Restarting therapy may require hospitalization.
- Advise patient to notify health care professional if signs of dehydration (vomiting, diarrhea, unable to drink normally, feeling faint) or bleeding (vomiting bright red blood, dark blood clots, or coffee ground-like material, black, tarry stools).
- Advise patient to notify health care professional if pregnancy is planned or suspected or if breast feeding.

Evaluation/Desired Outcomes
- Normalization of serum sodium levels. Therapy should be limited to 30 days.

Why was this drug prescribed for your patient?