Journal Academy Formulary (JACF)

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# Drug Review: Terlipressin

**Registrations:** It had been registered in the following countries**:** United Kingdom (UK), United States of America (USA), Canada, and Saudi Arabia (SA).

**Trade name (USA.);** TERLIVAZ ®

**Registration number (SA);** 11-367-07.

**Insurance Drug Formulary (SA);** Covered.

**General Information:**

**Registered Company:** Mallinckrodt hospital products inc.

**Regulatory Status:** RX.

**Mechanism of Action:**

Prodrug The active form is lysine vasopressin, the non-selective agonist of both V1 (smooth muscles of the arterial vasculature in the splanchnic region) and V2 receptors (collecting ducts of renal tubules).

**Indication**

**Approved (Labeled) indication:**

1. Type 1 hepatorenal syndrome (HRS-1).
2. The first line of therapy in managing acute variceal hemorrhage.
3. Control of hemorrhage.

**Route of Administration: Intravenous.**

**Dosage Forms:** Intravenous Powder for Solution: 0.85 MG.

**Dosing/Administration:**

Reconstitute each vial with 5 mL of NS to prepare a 0.85 mg/5 mL solution.

Administer through a peripheral or central line.

A dedicated central line is not required.

Flush the line after the administration.

**Dose:**

Control of hemorrhage

- (Variceal bleeding) Adjunct to endoscopic variceal band ligation, 2 mg IV bolus followed by 1 mg IV every 6 hr for 24 hr (off-label dosage).

Hepatorenal syndrome

- Initial, 0.85 mg IV (slow bolus injection over 2 min) every 6 hr on Days 1 through 3.

On day 4:

Continue the initial dosage if Serum Creatinine (SCr) has decreased by 30% or more significantly from baseline.

If SCr has decreased by less than 30% from baseline, increase the dosage to 1.7 mg IV every 6 hr.

If SCr remains at or above baseline, discontinue treatment.

- Duration of therapy, continue for a MAX of 14 days or until 24 hr following two consecutive SCr measurements of less than 1.5 mg/dL, drawn at least 2 hr apart.
- Initial, 1 mg IV bolus every 4 to 6 hr OR 2 mg/day as a continuous infusion; increase dosage stepwise (MAX of 12 mg/day) if SCr has not decreased by 25% from peak level after two days of treatment. Administer in combination with albumin.

**Dose in Renal/Hepatic Failure:** No dose adjustment is recommended.

**Geriatric Dose:** No dosage adjustment is needed.

**Adjustment required in a specific population:** No dose adjustment is recommended.

Indicated for pediatrics: Safety and effectiveness not established in pediatric patients.

**Pharmacokinetic:**

Distribution

- Vd: 6.3 L (lysine-vasopressin, 1370 L).

Metabolism

- Tissue peptidases.
- Lysine-vasopressin: Active.

Excretion

- Renal: Less than 1% (lysine-vasopressin, less than 0.1%).
- Total body clearance: 27.4 L/hr (lysine-vasopressin, 318 L/hr).

Elimination Half-Life:

- 0.9 hr (lysine-vasopressin, 3 hr).

**Safety:**

**Common Adverse Reactions (%):** abdominal pain, nausea, diarrhea, and dyspnea.

**Severe/rare adverse Reactions (%):** Ischemia and Respiratory failure (15.5%).

**Drug Interactions:** No significant drug-drug interactions are anticipated.

**Contraindications / Precautions:**

**Contraindications**

In patients experiencing hypoxia or worsening respiratory symptoms.

In patients with ongoing coronary, peripheral, or mesenteric ischemia.

**Precautions**

Avoid use in patients with a history of severe cardiovascular conditions, cerebrovascular and ischemic disease.

Adverse reactions such as respiratory failure and ischemia might make a patient ineligible for liver transplantation; consider the benefits and risks of administration in patients with high prioritization for liver transplantation.

Serious or fatal respiratory failure has been reported, and patients with fluid overload are at increased risk.

**Monitoring Requirements:**

**Before starting treatment:**

- Serum creatinine value: Baseline.
- Acute-on-Chronic Liver Failure Grade: Before treatment initiation.
- Oxygen saturation.
- Volume status: Before treatment initiation.

**During Treatment:**

Serum creatinine value: on day 4 of treatment.

Oxygen saturation.

**Sound-Alikes/ Look-Alikes:** Not available.

**High Alert:** Not available.

**Boxed warnings or alerts issue:**

Intravenous (Powder for Solution)

Fatal Respiratory Failure.

Do not initiate terlipressin in patients experiencing hypoxia until oxygenation levels improve, and discontinue terlipressin if SpO2 decreases below 90%.

**Toxicity if antidote required:** Not available.

**Storage if there is a special condition:**

**IV Rout:**

**a)** Store in the original carton in the refrigerator between 2 and 8°C and Protect from light.

b) If not used immediately, the reconstituted solution can be refrigerated between 2 and 8°C for 48 hr; do not freeze.

## Patient counseling

1. This Drug is unsafe during pregnancy.
2. If you have a history of lung or cardiac disease, tell your doctor.
3. Possible side effects: abdominal pain, nausea, diarrhea, and dyspnea.

## REFERENCES


1. TERLIVAZ intravenous injection (Terlipressin) [package inert]. Mallinckrodt Hospital Products Inc (per FDA). Bedminster, NJ; 2022.
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4. Kulkarni AV, Arab JP, Premkumar M, Benítez C, Tirumalige Ravikumar S, Kumar P, *et al.* Terlipressin has stood the test of time: clinical overview in 2020 and


## Cost Analysis

| Drugs | Drug classes | Approval Indication | Dose | Cost | Insurance drug formulary (SCHI) |
|---|---|---|---|---|---|
| Terlipressin | Endocrine-Metabolic Agent \| Genitourinary Agent. | The vasoconstrictor terlipressin is used for type 1 hepatorenal syndrome (HRS-1)and is the first line of therapy in treating acute variceal hemorrhage. | Control of hemorrhage (Variceal bleeding) Adjunct to endoscopic variceal band ligation, 2 mg IV bolus followed by 1 mg IV every 6 hr for 24 hr (off-label dosage). Hepatorenal syndrome<br>Initial, 0.85 mg IV (slow bolus injection over 2 min) every 6 hr on Days 1 through 3 (FDA dosage)<br>At day 4, if serum creatinine (SCr) has decreased by 30% or more significantly from baseline, continue the initial dosage (FDA dosage)<br>At day 4, if SCr has decreased by less than 30% from baseline, increase the dosage to 1.7 mg IV every 6 hr (FDA dosage)<br>At day 4, if SCr remains at or above baseline, discontinue treatment (FDA dosage)<br>Duration of therapy, continue for a MAX of 14 days or until 24 hr following two consecutive SCr measurements of less than 1.5 mg/dL, drawn at least 2 hr apart (FDA dosage)<br>Initial, 1 mg IV bolus every 4 to 6 hr OR 2 mg/day as a continuous infusion; increase the dosage stepwise (MAX of 12 mg/day) if SCr has not decreased by 25% from peak level after two days of treatment. Administer in combination with albumin (guideline dosage). | 5 MG =60 USD | Covered:<br>Glypressin 1mg Powder For IV Injection<br>Glypressin 0.1 Mg/Ml Solution For Injection. |
| Octreotide | Endocrine-Metabolic Agent | Acromegaly, Inadequate response to or ineligible for surgery, radiation, or bromocriptine mesylate<br>Acromegaly, Long-term maintenance with response to and tolerance of octreotide or lanreotide<br>Carcinoid syndrome, Metastatic; symptomatic treatment<br>Vasoactive intestinal peptide-secreting tumor, Associated diarrhea. | Acromegaly, Long-term maintenance with response to and tolerance of octreotide or lanreotide<br>Initial, 40 mg orally daily administered as 20 mg twice daily.<br>Bleeding esophageal varices<br>50 mcg IV bolus, then 50 mcg/hr IV continuously for 2 or 5 days with endoscopic therapy (off-label dosage)<br>carcinoid syndrome, Metastatic; symptomatic treatment<br>(Bynfezia Pen(TM)) Initial, 100 to 600 mcg subQ daily in 2 to 4 divided doses for two weeks (mean, 300 mcg/day). Drug-induced hypoglycemia, Sulfonylurea<br>75 mcg subQ plus 50 mL of 50% dextrose IV and oral carbohydrate<br>neuroendocrine tumor<br>30 mg long-acting repeatable depot injection IM every 28 days (off-label dosage). | $71.43 for 1, 5ML of 200MCG/ML Solution | Covered |


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