One in five adult female dogs suffers from urinary leaking, and for more than a decade veterinarians have trusted PROIN® (phenylpropanolamine hydrochloride) to control it. PROIN is the only FDA-approved medication for the treatment of urinary incontinence due to urethral sphincter hypotony.

PROIN is:
- **Proven** FDA-approved for control of urinary incontinence due to urethral sphincter hypotony
- **Convenient** Scored tablets are available in three sizes for precise dosing
- **Simple to Stock** Available from your distributor with no compounding required
- **Easy To Administer** Chewable, liver-flavored tablets improve compliance

**With continued dosing for 180 days, PROIN achieved 98.1% owner satisfaction for the control of urinary incontinence.²**

“P is for PROIN and PROIN is for Pee”

PRN® Pharmacal | 8809 Ely Road | Pensacola, FL 32514 | 800.874.9764 | prnpharmacal.com/proin

PROIN® (phenylpropanolamine hydrochloride) Chewable Tablets

For oral use in dogs only

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Description: PROIN® (phenylpropanolamine hydrochloride) is a sympathomimetic amines class related to ephedrine. Phenylpropanolamine hydrochloride (PPA) is the stereoisomer designated as (S)-alpha-methylamino-1-phenylpropane (3S*, 3′R*, 4S*, 4′R*). The empirical formula is C₁₀H₁₅NO₂·HCl and the molecular weight is 187.67. It is a white crystalline compound having a slight astringent odor. PPA is freely soluble in water and alcohol but practically insoluble in either, benzene and chloroform. The chemical structure of phenylpropanolamine hydrochloride is:

![Chemical Structure](image)

Indication: PROIN® is indicated for the control of urinary incontinence due to urinthal sphincter hypotension in dogs. 

Dosage and Administration: The total recommended dosage for oral administration is 2 mg/kg (or 0.91 mg/lb) of body weight twice daily. PROIN is scored and dosage should be calculated in half-tablet increments.


Precautions: PROIN may cause increased thirst; therefore, provide ample fresh water.

Overdose has been associated with dogs chewing through closed bottles of PROIN and consuming multiple tablets. Therefore, it is important to store PROIN Chewable Tablets out of reach of dogs and other pets in a secured location.

Use in dogs with incontinence due to a urinary tract infection will mask symptoms. PROIN is not effective in dogs with incontinence due to neurologic disease or malnutrition.

PROIN may cause hypertension; therefore, use with caution in dogs with pre-existing heart disease, hypertension, liver disease, kidney insufficiency, diabetes, glaucoma, and with a condition with a predilection for hypertension. Use with caution in dogs receiving sympathetic drugs, tricyclic antidepressants, or monoamine oxidase inhibitors as increased toxicity may result. Use with caution in dogs administered phenylpropionate-alkanes such as this may increase the risk of cardial arrhythmias.

A laboratory study in human blood revealed that PPA and in conjunction with aspirin may potentially decrease platelet aggregation 1.

The safe use of PROIN in dogs used for breeding purposes, during pregnancy or in lactating bitches, has not been evaluated.

Adverse Reactions: “Pre Approval Experience”: A placebo-controlled clinical study involving 123 PROIN-treated dogs and 61 placebo-treated dogs was conducted for 28 days. The most common adverse reactions are shown in Table 1 below. In addition, one dog exhibited dissemination, nematossus, a 7.7% loss of body weight, and hypertension with proteinuria. A second dog exhibited restless behavior, lethargy, a 2.8% body weight loss, and proteinuria, and precipitate. 

Table 1: Number and percentage of dogs with adverse reactions in the 28-day placebo-controlled clinical study

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>PROIN-treated (N=123)</th>
<th>Placebo-treated (N=61)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emesis</td>
<td>20.3%</td>
<td>8.2%</td>
</tr>
<tr>
<td>Hypertension (≥ 160 mmHg)</td>
<td>19.5%</td>
<td>14.7%</td>
</tr>
<tr>
<td>Anorexia</td>
<td>16.3%</td>
<td>3.3%</td>
</tr>
<tr>
<td>Body weight loss (&gt;50%)*</td>
<td>16.1%</td>
<td>6.8%</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>13.0%</td>
<td>8.2%</td>
</tr>
<tr>
<td>Anxiety/aggression/change</td>
<td>9.7%</td>
<td>3.2%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>7.3%</td>
<td>8.9%</td>
</tr>
<tr>
<td>Polydipsia</td>
<td>6.5%</td>
<td>9.8%</td>
</tr>
<tr>
<td>Lethargy</td>
<td>5.7%</td>
<td>1.8%</td>
</tr>
<tr>
<td>Musculoskeletal Disorder</td>
<td>3.2%</td>
<td>1.6%</td>
</tr>
<tr>
<td>Insomnia/episode disorder</td>
<td>2.5%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Anxiety/behavior change/Gagging</td>
<td>5.7%</td>
<td>5.7%</td>
</tr>
</tbody>
</table>

One hundred seventy-five dogs continued into the 6-month open-label clinical study conducted in 21 study sites across the U.S. All the dogs had participated in the 28-day placebo-controlled clinical and had urinary incontinence due to urothelial hypotension. Dogs were administered PROIN hourly twice daily for 180 days. PROIN was effective for the control of urinary incontinence for 180 days based on 98.1% owner satisfaction. The dogs averaged 0.43 accidents per dog per week. Changes in hematology and serum chemistry were not considered clinically significant or related to treatment.

Table 2: Mean urinary accidents per week by treatment group, females

<table>
<thead>
<tr>
<th>Week</th>
<th>Mean Urinary Accidents (PROIN, N=64)</th>
<th>Mean Urinary Accidents (Placebo, N=36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.9</td>
<td>4.8</td>
</tr>
<tr>
<td>2</td>
<td>2.5</td>
<td>4.1</td>
</tr>
<tr>
<td>3</td>
<td>3.1</td>
<td>3.1</td>
</tr>
<tr>
<td>4</td>
<td>1.6</td>
<td>2.6</td>
</tr>
</tbody>
</table>

Adverse Reactions: “Post Approval Experience”:

One-hundred thirty dogs continued into the 6-month open-label clinical study conducted in 21 study sites across the U.S. All the dogs had participated in the 28-day placebo-controlled clinical and had urinary incontinence due to urothelial hypotension. Dogs were administered PROIN hourly twice daily for 28 days. PROIN was effective for the control of urinary incontinence based on a decrease in urinary accidents per week. Changes in hematology and serum chemistry were not considered clinically significant or related to treatment.

Table 3: Mean urinary accidents per week by treatment group, females

<table>
<thead>
<tr>
<th>Week</th>
<th>Mean Urinary Accidents</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.9</td>
</tr>
<tr>
<td>2</td>
<td>2.5</td>
</tr>
<tr>
<td>3</td>
<td>3.1</td>
</tr>
<tr>
<td>4</td>
<td>1.6</td>
</tr>
</tbody>
</table>

For a copy of the Safety Data Sheet (SDS) or to report suspected adverse drug events, contact Pegasus Laboratories at 1-888-674-9764. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FOA-VETS or http://www.fsa.usda.gov/ Veterinarian/ VeterinaryHealth. 

Information for Owner or Person Treating Animal: Always follow the dosage instructions for PROIN provided by your veterinarian. Monitor your dog after giving PROIN to see if any of all is consumed. If you have difficulty giving PROIN, contact your veterinarian. It may take several days of treatment with PROIN before urinary incontinence improves. If you notice a dog lose weight, give it as soon as you remember. If it is close to the time for the next dose, skip the dose you missed and go back to the regular dosage schedule. Do not give two doses at once. PROIN should only be given to dogs for which it was prescribed. Because PROIN is flavoured, store in a secure area.

Dogs may willingly consume more than the recommended dosage of PROIN Chewable Tablets. Instead of dogs chewing through closed bottles of PROIN and eating the bottle contents have been reported. Keep the product in a secured storage area out of the reach of pets in order to prevent accidental ingestion or overdose. Contact your veterinarian immediately if the dog ingests more than tablets prescribed or if other pets ingested PROIN Chewable Tablets. In the case of accidental ingestion by humans, contact a physician immediately.

Contact your veterinarian if you notice restlessness or irritability, loss of appetite, the incontinence persists or worsens, or any other unusual signs. Consult your veterinarian before using PROIN with any other medications.

Clinical Pharmacology: Phenylpropanolamine is a chemical analog of the endogenous sympathetic amines. It is a urodynamic agent which is reported to increase urethral tone in dogs. Its mechanism of action is not well determined, but it is believed to cause the release of norepinephrine by indirectly stimulating both the alpha and beta-adrenergic receptors of the smooth muscle to increase smooth muscle tone of the urethra, bladder neck, and the internal urethral sphincter.

The pharmacokinetics of phenylpropanolamine in dogs has not been well studied. In humans, phenylpropanolamine is rapidly absorbed after oral administration of solid dosage forms and has an area of approximatley 15-30 minutes and duration of about three hours. In a published study in dogs, phenylpropanolamine disposition was characterized in three dogs administered phenylpropanolamine intravenously and orally in immediate-release and controlled-release formulation. 2 The terminal elimination half-life averaged 3.1 ± 0.05 hours after the intravenous dose. Oral absorption from the immediate-release capsule was rapid and bioavailability was 96.2 ± 6.7%. Absorption of phenylpropanolamine from the controlled-release capsule was 91.7 ± 5.9%

Effectiveness: A 28-day placebo-controlled clinical study was conducted in 21 study sites across the U.S. The study included 104 dogs with urinary incontinence due to urinary hypercontractility of which 127 dogs (100 female, 27 male) were evaluated for effectiveness. Dogs were randomly assigned either to receive 2 mg/kg of PROIN (121 dogs) or placebo (61 dogs) administered orally twice daily for 28 days. PROIN was effective in controlling urinary incontinence based on a decrease in urinary accidents per week. Changes to hematology and serum chemistry were not considered clinically significant or related to treatment.


NADA #141-324, Approved by FDA.

How Supplied: 

PROIN® is a registered trademark of Pegasus Laboratories, Inc.

Pensacola, FL 32514, USA

References:


Manufactured by: Pegasus Laboratories, Inc.

An Employee-Owned Company

Pensacola, FL 32514, USA

11-2014