EPANED®
(enalapril maleate) Oral Solution

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FULL PRESCRIBING INFORMATION

WARNING: THERAPEUTIC USES
See FULL PRESCRIBING INFORMATION for complete prescribing information. See Also PRECAUTIONS: General, Dose Adjustments for Renal or Impaired Hepatic Function, Postmarketing Experience, Patient Counseling

1 INDICATIONS AND USAGE
1.1 Treatment of hypertension
Hypertension

- treatment of symptomatic heart failure (1.2).

- treatment of hypertension in adults and children 

1.2 Treatment of symptomatic heart failure

- Low dose EPANED is indicated for the treatment of symptomatic heart failure, usually in combination with diuretics and digitalis.

Full prescribing information: CONTENTS*

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1.2 Treatment of symptomatic heart failure

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2.1 Hypertension

- EPANED is indicated for the treatment of systolic hypertension, usually in combination with diuretics and digitalis.

2.2 Heart Failure

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3 ADVERSE REACTIONS

3.1 Hypotension

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3.2 Angioedema

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6.1 Pregnancy

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6.2 Lactation

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Adverse Reactions Occurring in Greater Than 1% of Patients With Hypertension

| Side Effects | Discontinuation | [see Dosage and Administration (2.1)] |
|-------------|----------------|
| Hypokalemia | 7.9 percent versus 0.6 percent in placebo. |
| Dizziness | 7.9 percent versus 0.6 percent in placebo. |
| Headache | 7.9 percent versus 0.6 percent in placebo. |
| Fatigue | 7.9 percent versus 0.6 percent in placebo. |
| Constipation | 7.9 percent versus 0.6 percent in placebo. |

Other adverse reactions that occurred in more than 1% of patients treated with enalapril maleate (both dosages combined) and placebo were as follows. | [see Dosage and Administration (2.1)] |
<table>
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In some patients achieving optimal blood pressure reduction may require several months of therapy. The antihypertensive effects of enalapril may be more evident after long-term therapy. Abrupt withdrawal of enalapril has been associated with a rapid increase in blood pressure.

In hypertensive studies in patients with essential hypertension, blood pressure reduction was accompanied by a reduction in peripheral arterial resistance with an increase in cardiac output and little or no change in heart rate. In hemodynamic studies in patients with left ventricular dysfunction, enalapril caused a reduction in mean arterial pressure and pulmonary artery wedge pressure, and heart rate, and increased cardiac output and stroke volume.

Enalapril and enalaprilat have been detected in human breast milk. Because of the potential for severe adverse reactions in nursing infants, the possibility of milk feeding should be considered before enalapril is administered to a nursing woman.

The SOLVD trials were not designed to determine whether treatment of asymptomatic patients with low ejection fraction modified the progression of underlying heart disease. In another multination, randomized controlled trial (CONSENSUS II) limited to patients with NYHA Class II congestive heart failure and negative or medicated antianginal medications, use of enalapril was associated with improved survival. The results are shown in the following table.

### CONSENSUS II Survival Rates

<table>
<thead>
<tr>
<th>Ejection Fraction (%)</th>
<th>0%</th>
<th>0.1-30%</th>
<th>31-49%</th>
<th>50-70%</th>
</tr>
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<tbody>
<tr>
<td>12-Month Survival (%)</td>
<td>96%</td>
<td>90%</td>
<td>80%</td>
<td>55%</td>
</tr>
</tbody>
</table>

# 13.2 Pharmacokinetics

A multiple dose pharmacokinetics study was conducted in 41 hypertensive women and hypertensive patients aged 12-65 years, treated with enalapril maleate 2.5 mg once daily for 16 weeks as monotherapy. Mean increases in serum potassium were 0.33 mmol/L (0.75 mEq/L).

### 13.3 Animal Toxicology and/or Pharmacology

Trifluoperazine and chlorpromazine were administered to experimental animals including rats and dogs to determine the potential for enalapril to cause QTc interval prolongation. There was no evidence of a tumorigenic effect when enalapril was administered for 106 weeks to male and female rats.

# 14. CLINICAL STUDIES

### 14.1 Heart Failure, Medical Trials

Enalapril is a nonprescription medication used to treat hypertension, left ventricular dysfunction, and heart failure. It is available as a tablet, capsule, and solution. Enalapril works by blocking the renin-angiotensin-aldosterone system (RAAS), which helps regulate blood pressure.

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