HEMANGEOL® (propranolol hydrochloride oral solution) 4.28 mg/mL

HIGHLIGHTS OF PRESCRIBING INFORMATION

INDICATIONS AND USAGE
HEMANGEOL® is indicated for the treatment of proliferating infantile hemangiomas requiring systemic therapy (“postnatal weeks 1 to 12”).

DOSEAGE AND ADMINISTRATION
- Initiate treatment at ages 5 weeks to 5 months.
- Starting dose is 0.15 mL/kg (0.6 mg/kg) twice daily. After 1 week, increase dose by 0.05 mL/kg (0.2 mg/kg) twice daily, as needed, based on clinical response and tolerability.
- Initiate treatment at ages 6 months to 12 months.
- Starting dose is 0.15 mL/kg (0.6 mg/kg) twice daily. After 1 week, increase dose by 0.05 mL/kg (0.2 mg/kg) twice daily, as needed, based on clinical response and tolerability.

CONTRAINDICATIONS
- Patients with known hypersensitivity to any component of HEMANGEOL.
- Patients who are not able to eat

DOSEAGE FORMS AND STRENGTHS
- Oral solution: 4.28 mg/mL propranolol hydrochloride (3)

CONTRAINDICATIONS
- Patients with known hypersensitivity to any component of HEMANGEOL.

DOSEAGE AND ADMINISTRATION
- Orally disintegrating tablets: 6.5 mg propranolol hydrochloride (2)

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Propranolol hydrochloride is a synthetic beta-adrenergic receptor blocking agent primarily used to treat hypertension, angina pectoris, and other indications. It is also an effective treatment for infantile hemangiomas (IH) and a number of other conditions, including pheochromocytoma, tachyarrhythmias, and mitral valve prolapse.

### Pharmacology

**Absorption:**
Propranolol hydrochloride is rapidly and completely absorbed from the gastrointestinal tract. Peak plasma concentrations appear about 1 to 4 hours after an oral dose. Administration of protein-rich foods increases the bioavailability of propranolol.

**Distribution:**
Propranolol is extensively distributed to tissues and tissues, with a high degree of binding to plasma proteins. It is also highly bound to red blood cells, with about 70% of the plasma concentration in erythrocytes.

**Metabolism:**
Propranolol undergoes extensive metabolism in the liver. The principal pathways of metabolism include oxidation (mainly 4-hydroxylation), N-dealkylation followed by further side-chain oxidation, and glucuronidation. The four major final metabolites are propranolol glucuronide, propranolol N-oxide, hydroxymethylpropranolol, and hydroxyethylpropranolol. stools.

**Excretion:**
About 90% of a dose is excreted as unchanged drug in the urine. The remainder is excreted as metabolites.

### Clinical Pharmacology

**Impact of propranolol on co-administered drugs:**
Propranolol interacts with a number of co-administered drugs, including nonsteroidal anti-inflammatory drugs (NSAIDs), beta-adrenergic blocking agents, calcium channel blockers, and amide anesthetics. The effect of propranolol on plasma concentrations of co-administered drugs is summarized in the table below.

<table>
<thead>
<tr>
<th>Co-administered Drug</th>
<th>Effect on Plasma Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>Decrease</td>
</tr>
<tr>
<td>Verapamil</td>
<td>Increase 80%</td>
</tr>
<tr>
<td>Nifedipine</td>
<td>Increase 50%</td>
</tr>
<tr>
<td>Propafenone</td>
<td>Increase</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Increase (acute use), decrease (chronic use)</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>Increase 70%</td>
</tr>
<tr>
<td>Nisoldipine</td>
<td>Increase 50%</td>
</tr>
<tr>
<td>Diazepam</td>
<td>No change</td>
</tr>
<tr>
<td>Thioridazine</td>
<td>Increase 200%</td>
</tr>
<tr>
<td>Chlorothiazide</td>
<td>No change</td>
</tr>
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### STABILITY

Propranolol hydrochloride is a stable, white, crystalline solid with a molecular weight of 297.71 g/mol. It is stable under the conditions of normal storage and handling.

### CONTRAINDICATIONS

Propranolol is contraindicated in patients with a history of hypersensitivity to any component of the formulation or to other beta-adrenergic blocking agents. It is also contraindicated in patients with sick sinus syndrome, AV block, severe bradycardia, and those with close AV nodal conduction (e.g., patients with documented paroxysmal atrial fibrillation). Additionally, it is contraindicated in patients with asthma or other bronchial, gastrointestinal and genitourinary symptoms, or those with a history of allergy to the use of beta-blockers.

### DOSAGE AND ADMINISTRATION

Propranolol hydrochloride is available in several dosage forms, including tablets, capsules, and injectable solutions. The dosage and administration of propranolol should be individualized based on the patient's response and the clinical condition. The usual adult dosage is 40-120 mg/day in divided doses. For children, the recommended starting dose is 2 mg/kg/day in 1.1 mg/kg/day increments at weekly intervals. At steady state, following administration of 3.4 mg/kg/day twice daily, peak plasma propranolol concentrations are reached in 1-2 hours and remain constant for at least 12 hours. The plasma propranolol concentration is presented in the table below.

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### ADVERSE REACTIONS

The hypotensive effect of MAO inhibitors and tricyclic antidepressants may be potentiated by co-administration of propranolol, which may increase the risk of orthostatic hypotension. The hypotensive effect of beta-blockers is an extension of their therapeutic effects: decreased heart rate, decreased cardiac output, and blood pressure. The hypotensive effect is most pronounced in patients with minimal cardiac reserve. A decrease in cardiac output, although not usually associated with symptoms, may precipitate frank heart failure in patients with pre-existing congestive heart failure. The hypotensive effect may also be potentiated by other drugs with positive inotropic effects, such as dopamine or dobutamine.

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