**CONTRAINDICATIONS**

- Severe brachiocephalic obstruction
- Left heart failure
- Congestive heart failure
- Pre-excitation syndromes
- Hypersensitivity to esmolol
- Second- or third-degree atrioventricular block
- Cardiogenic shock
- Decompensated heart failure
- Known hypersensitivity to esmolol
- Cardiac arrest
- Severe bradycardia, sinus pause, sinoatrial block, atrioventricular block, hypotension

**Additional Loading Doses**

Additional loading doses may be administered upon the physician's discretion. The following loading doses are typical when using esmolol for the indicated acute conditions:

- Sinus tachycardia: 50 mcg per kg per minute for gradual control (150 mcg per kg per minute in the setting of pheochromocytoma)
- New onset atrial fibrillation: 50 mcg per kg per minute for gradual control
- Premature ventricular contractions: 10 mcg per kg per minute
- Atrial flutter: 1 mcg per kg per minute
- Atrial fibrillation: 1 mcg per kg per minute

**DOSAGE AND ADMINISTRATION**

**Adults**

- Esmolol hydrochloride is administered by continuous intravenous infusion.
- The initial dose is 5 mcg per kg per minute. The dose may be titrated upward until the desired clinical effect is achieved. The maximum recommended dose is 200 mcg per kg per minute. Esmolol hydrochloride may be administered at a rate of 10 mcg per kg per minute or higher if needed and tolerated.

**Monitoring**

- During continuous intravenous administration, the blood pressure, heart rate, and oxygen saturation should be regularly monitored. Continuous electrocardiographic (ECG) monitoring is recommended. In patients with severe bradycardia, sinus pause, sinoatrial block, atrioventricular block, or hypotension, the effect of antidiabetic agents (blood glucose–lowering) may be potentiated.

- In hypoglycemic patients, or diabetic patients (especially those with autonomic neuropathy), exogenous short-acting insulin may raise blood glucose levels at some time points. Digoxin does not affect esmolol hydrochloride levels. If esmolol hydrochloride is used in the setting of pheochromocytoma, give 10 mcg per kg per minute until the esmolol hydrochloride infusion rate by one-half (50%).

- In patients with hypoglycemia, or diabetic patients (especially those with autonomic neuropathy), exogenous short-acting insulin may raise blood glucose levels at some time points. Digoxin does not affect esmolol hydrochloride levels. If esmolol hydrochloride is used in the setting of pheochromocytoma, give 10 mcg per kg per minute until the esmolol hydrochloride infusion rate by one-half (50%).

- If severe hypotension develops, reduce or stop esmolol hydrochloride.

- Cardiac Failure

- Patients with cardiac failure may be at increased risk of developing potentially life-threatening hyperkalemia in hemodialysis patients. Monitor for signs of myocardial ischemia when discontinuing esmolol hydrochloride.

- Abrupt Discontinuation of Esmolol Hydrochloride

The abrupt discontinuation of esmolol hydrochloride therapy may be life-threatening in some patients with cardiac failure. Esmolol hydrochloride may aggravate peripheral circulatory disorders.

- Mitral Valve Prolapse

Patients with mitral valve prolapse are at increased risk of developing potentially life-threatening hyperkalemia in hemodialysis patients. Monitor for signs of myocardial ischemia when discontinuing esmolol hydrochloride.

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8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Esmolol hydrochloride has been shown to produce increased fetal
respiration and maternal uterine activity in rabbits given doses of
approximately 50 mg/kg/min. In two multicenter, randomized, double-blind,
controlled comparisons of esmolol hydrochloride with placebo, maternal
blood pressure was increased by 5% and maternal heart rate decreased by
15% compared to placebo in 600 patients. Esmolol hydrochloride was
administered at a rate of 100 mcg/kg/min to 100 patients with severe
hypertension, 150 mcg/kg/min to 100 patients with hypertension and 200
mcg/kg/min to 100 patients with mild hypertension. Esmolol hydrochloride
administered at 150 mcg/kg/min was found to be effective in decreasing
hypertension in human subjects.

Esmolol hydrochloride is a beta 1-selective (cardioselective) adrenergic
receptor-blocking agent. Unlike other beta-adrenergic blocking agents, it
has no intrinsic sympathomimetic activity and causes no significant
adrenergic rebound after abrupt withdrawal.

8.2 Labor and Delivery

In human electrophysiology studies, esmolol hydrochloride produced
a significantly larger fall in systolic blood pressure compared to placebo.
No adverse pulmonary effects were noted, and no change in the
percentages of patients experiencing dry air-induced bronchospasm.

In clinical studies of esmolol hydrochloride, there was no evidence of
significant fetal or neonatal toxicity. However, because of its effects on
maternal blood pressure and cardiac output, use during labor and delivery
should be reserved for those in which the potential benefit justifies the
potential risk to the fetus.

8.3 Nursing Mothers

Esmolol hydrochloride is distributed into breast milk. The drug
concentrations in breast milk were lower than those achieved in plasma.
Maternal plasma concentrations in the range of 1 to 4.3 mcg/mL were
related to milk concentrations in the range of 0.02 to 0.14 mcg/mL.

Breastfeeding mothers who require esmolol hydrochloride should be
instructed to either discontinue their breast feeding or not to receive
esmolol hydrochloride.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Receptors located chiefly in cardiac muscle, but this preferential
effect is not absolute and at higher doses it begins to inhibit beta 2
receptors located in vascular smooth muscle. Esmolol hydrochloride
produced a significantly larger fall in systolic blood pressure compared to
placebo.

8.4 Pediatric Use

In general, dose selection for an elderly patient should usually
be governed by the general principles of pharmacokinetics and
pharmacodynamics of the drug and the condition being treated.

8.5 Geriatric Use

Because of its short term usage no carcinogenicity or reproductive
toxicity studies have been conducted with esmolol hydrochloride.

8.6 Hepatic Impairment

In patients with hepatic impairment no special precautions are
necessary. In patients with renal impairment, the drug is not
excreted unchanged by the kidneys, but is eliminated by the liver, and
active drug concentrations may be doubled in the urine of patients
with severe renal impairment. In general, dose selection for patients
with severe renal impairment should be guided by the general principles
of pharmacokinetics and pharmacodynamics of the drug and the
condition being treated.

8.7 Renal Impairment

There are no specific precautions necessary. However, patients who
are receiving concomitant digoxin should be monitored for hypotension.

12.2 Pharmacodynamics

The acid metabolite has an elimination half-life of about 3.5 hours.

8.5.1 Signs and Symptoms of Overdose

Patients who have received intravenous propranolol, and at a dosage
of 1 mg, two

12.3 Pharmacokinetics

The elimination half-life of esmolol hydrochloride was decreased
from 2.5 hours in healthy volunteers to 1 hour in patients with severe
hypertension. In patients with severe hypertension, the AUC increased
by 15% compared to healthy volunteers.

8.4.1 Esmolol Hydrochloride

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hypertension. In patients with severe hypertension, the AUC increased
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8.8.1 Glucagon

Glucagon is a potent stimulator of beta 1-receptors located in cardiac
muscle. It causes an increase in heart rate and cardiac output.

8.8.2 Autonomic Nervous System

The autonomic nervous system consists of two branches, the parasympathetic
and sympathetic nervous systems. The parasympathetic nervous system

12.5.4 In Vitro Studies

The in vitro studies were conducted on cultured cells, and the data
obtained should be interpreted with caution.

12.5.5 In Vivo Studies

The in vivo studies were conducted in animal models and the results
should be interpreted with caution.

150 mcg/kg/min, approximated endogenous levels and were less than
20 to 50% of patients, identified either as adverse reaction reports
or renal blood flow. Esmolol has a rapid distribution half-life of about 2
minutes and a rapid plasma clearance of about 200 minutes.

Esmolol hydrochloride has been shown to be effective in decreasing
hypertension in human subjects.

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