ENLON®
(edrophonium chloride injection, USP)
150 mg/15 mL

DESCRIPTION
ENLON is a short and rapid-acting cholinergic drug. Chemically, edrophonium chloride is ethyl(m-hydroxyphenyl) dimethylammonium chloride and its structural formula is:

Each mL contains, in a sterile solution, 10 mg edrophonium chloride compounded with 0.45% phenol as a preservative, and 0.2% sodium sulfite as an antioxidant, buffered with sodium citrate and citric acid, and pH adjusted to approximately 5.4.

ENLON is intended for IV and IM use.

CLINICAL PHARMACOLOGY
ENLON is an anticholinesterase drug. Its pharmacologic action is due primarily to the inhibition or inactivation of acetylcholinesterase at sites of cholinergic transmission. Its effect is manifest within 30 to 60 seconds after injection and lasts an average of 10 minutes.

Pediatric Pharmacology: The pharmacology of edrophonium chloride was studied in 14 infants (between 3 weeks and 11 months old) and 12 children (between 1 year and 6 years old) during a steady-state infusion of d-tubocurarine during N₂O-halothane anesthesia and controlled ventilation for elective surgery.¹ The ED₅₀ dose (dose producing 50% antagonism of 90% neuromuscular depression) for edrophonium chloride was 145 mcg/kg in infants and 233 mcg/kg in children not significantly different from that observed in adult patients; however, there was greater variability among infants and children than adults. Time to peak antagonism and duration of antagonism were similar between the two pediatric age groups and adult patients. Edrophonium chloride pharmacokinetics were studied in four infants (3 months through 7 months of age) and four children (1 through 4 years of age). Total clearance was 17.8 mL/kg/min in infants and 14.2 mL/kg/min in children. Total clearance was significantly greater in infants than in adults (8.3 ± 2.9 mL/kg/min p<0.05. Elimination half-life was 73 ± 30 minutes in infants and 99 ± 31 minutes in children compared with 126 ± 59 minutes in adults. Volume of distribution in infants and children was 1.18 ± 0.20 L/kg and 1.22 ± 0.74 L/kg, respectively, compared with 0.90 ± 0.13 L/kg in adults.

INDICATIONS AND USAGE
ENLON is recommended for the differential diagnosis of myasthenia gravis and as an adjunct in the evaluation of treatment requirements in this disease. Because of its brief duration of action, it is not recommended for maintenance therapy in myasthenia gravis.

ENLON is also useful whenever a curare antagonist is needed to reverse the neuromuscular block produced by curare, tubocurarine, gallamine triethiodide or dimethyl-tubocurarine. It is not effective against decamethonium bromide and succinycholine chloride. It may be used adjunctively in the treatment of respiratory depression caused by curare overdose.

CONTRAINDICATIONS
Known hypersensitivity to anticholinesterase agents; intestinal and urinary obstructions of mechanical type.

WARNINGS
Whenever anticholinesterase drugs are used for testing, a syringe containing 1 mg of atropine sulfate should be immediately available to be given in aliquots intravenously to counteract severe cholinergic reactions which may occur in the hypersensitive individual, whether he is normal or myasthenic. ENLON should be used with caution in patients with bronchial asthma or cardiac dysrhythmias. The transient bradycardia which sometimes occurs can be relieved by atropine sulfate. Isolated instances of cardiac and respiratory arrest following administration of ENLON have been reported. It is postulated that these are vagotonic effects.

ENLON contains sodium sulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthma-like episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

Usage in Pregnancy: The safety of ENLON during pregnancy or lactation in humans has not been established. Therefore, use of ENLON in women who may become pregnant requires weighing the drug’s potential benefits against its possible hazards to mother and child.

PRECAUTIONS
Patients may develop “anticholinesterase insensitivity” for brief or prolonged periods. During these periods the patients should be carefully monitored and may need respiratory assistance. Dosages of anticholinesterase drugs should be reduced or withheld until patients again become sensitive to them.

Pediatric Use:
The safety and effectiveness of edrophonium chloride in the differential diagnosis of myasthenia gravis have been established in pediatric patients.

OVERDOSAGE
With drugs of this type, muscarine-like symptoms (nausea, vomiting, diarrhea, sweating, increased bronchial and salivary secretions and bradycardia) often occur with overdose (cholinergic crisis). An important complication that can arise is obstruction of the airway by bronchial secretions. These may be managed with suction (especially if tracheostomy has been performed) and by the use of atropine. Many experts have advocated a wide range of doses of atropine (for ENLON, see atropine dosage below), but if there are copious secretions, up to 1.2 mg intravenously may be given initially and repeated every 20 minutes until secretions are controlled. Signs of atropine overdose such as dry mouth, flush and tachycardia should be avoided as.

ADVERSE REACTIONS
Careful observation should be made for severe cholinergic reactions in the hyperreactive individual. The myasthenic patient in crisis who is being tested with ENLON should be observed for bradycardia or cardiac standstill and cholinergic reactions if an overdose is given.

The following reactions common to anticholinesterase agents may occur, although not all of these reactions have been reported with the administration of ENLON, probably because of its short duration of action and limited indications:

Eye: Increased lacrimation, pupillary constriction, spasm of accommodation, diplopia, conjunctival hyperemia.

CNS: Convulsions, dysarthria, dysphonia, dysphagia.

Respiratory: Increased tracheobronchial secretions, laryngospasm, bronchiolar constriction, paralysis of muscles of respiration, central respiratory paralysis.

Cardiac: Arrhythmias (especially bradycardia), fall in cardiac output leading to hypotension.

G.I.: Increased salivary, gastric and intestinal secretion, nausea, vomiting, increased peristalsis, diarrhea, abdominal cramps.

Skeletal Muscle: Weakness, fasciculations.

Miscellaneous: Increased urinary frequency and incontinence, diaphoresis.

DRUG INTERACTIONS
Care should be given when administering this drug to patients with symptoms of myasthenic weakness who are also on anticholinesterase drugs. Since symptoms of anticholinesterase overdose (cholinergic crisis) may mimic underdosage (myasthenic weakness), their condition may be worsened by the use of this drug. (See OVERDOSAGE section for treatment.)

EDROPHONIUM CHLORIDE INJECTION, USP
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tendous secretions and bronchial plugs may form. A total dose of atropine of 5 to 10 mg or even more may be required. The following steps should be taken in the management of overdosage of ENLON:

1. Adequate respiratory exchange should be maintained by assuring an open airway and the use of assisted respiration augmented by oxygen.
2. Cardiac function should be monitored until complete stabilization has been achieved.
3. Atropine sulfate in doses of 0.4 to 0.5 mg should be administered intravenously. This may be repeated every 3 to 10 minutes. Because of the short duration of action of ENLON the total dose required will seldom exceed 2 mg.
4. If convulsions occur or shock is present, appropriate measures should be instituted.

**DOSEAGE AND ADMINISTRATION**

ENLON Test in the Differential Diagnosis of Myasthenia Gravis

**Intravenous Dosage (Adults):** A tuberculin syringe containing 1 mL (10 mg) of ENLON is prepared with an intravenous needle, and 0.2 mL (2 mg) is injected intravenously within 15 to 30 seconds. The needle is left in situ. Only if a cholinergic reaction (muscarnic side effects, skeletal muscle fasciculations and increased muscle weakness) occurs after injection of 0.2 mL (2 mg), the test is discontinued and atropine sulfate, 0.4 mg to 0.5 mg, is administered intravenously. After one-half hour the test may be repeated.

**Intramuscular Dosage (Adults):** In adults with inaccessible veins, dosage for intramuscular injection is 1 mL (10 mg) of ENLON. Subjects who demonstrate hyperreactivity to this injection (cholinergic reaction), should be retested after one-half hour with 0.2 mL (2 mg) of ENLON intramuscularly to rule out false-negative reactions.

**Dosage in Pediatric Patients:** The intravenous testing dose of ENLON in pediatric patients weighing up to 75 lbs is 0.1 mL (1 mg); above this weight, the dose is 0.2 mL (2 mg). If there is no response after 45 seconds, it may be repeated up to 0.5 mL (5 mg) in pediatric patients under 75 lbs, given in increments of 0.1 mL (1 mg) every 30 to 45 seconds and up to 1 mL (10 mg) in heavier patients. In infants, the recommended dose is 0.05 mL (0.5 mg). Because of technical difficulty with intravenous injection in pediatric patients, the intramuscular route may be used. In pediatric patients weighing up to 75 lbs, 0.2 mL (2 mg) is injected intramuscularly. In pediatric patients weighing more than 75 lbs, 0.5 mL (5 mg) is injected intramuscularly. All signs which would appear with the intravenous test appear with the intramuscular test except that there is a delay of 2 to 10 minutes before a reaction is noted.

**ENLON Test for Evaluation of Treatment Requirements in Myasthenia Gravis:** The recommended dose is 0.1 mL to 0.2 mL (1 mg to 2 mg) of ENLON, administered intravenously 1 hour after oral intake of the drug being used if no reaction occurs. If the intravenous test is negative, the remaining 0.1 mL (1 mg) can be injected. If no improvement occurs after 0.2 mL (2 mg) dose, it is usually wisest to discontinue all anticholinesterase drug therapy and secure controlled ventilation by tracheostomy with assisted respiration.

**For use as a Curare Antagonist:** ENLON should be administered by intravenous injection in 1 mL (10 mg) doses given slowly over a period of 30 to 45 seconds so that the onset of cholinergic reaction can be detected. This dosage may be repeated whenever necessary. The maximal dose for any one patient should be 4 mL (40 mg). Because of its brief effect, ENLON should not be given prior to the administration of curare, tubocurarine, gallamine triethiodide or dimethyl-tubocurarine. It should be used at the time when its effect is needed. When given to counteract curare overdosage, the effect of each dose on the respiration should be carefully observed before it is repeated, and assisted ventilation should always be employed.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

**H ow Supplied**

ENLON (edrophonium chloride injection, USP):

- 15 mL Multiple-Dose Vial

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Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.]

**References**


Enlon is a registered trademark of Mylan Teoranta.