Pradox

Pralidoxime Chloride

COMPOSITION

Pradox Injection : Each vial contains Pralidoxime Chloride USP 1000 mg.

PHARMACOLOGICAL INFORMATION

Pralidoxime Chloride is a acetylcholinesterase reactivator. The principal action of Pralidoxime Chloride is to reactivate acetylcholinesterase (mainly outside of the central nervous system) which has been inactivated by phosphorylation due to an organophosphate pesticide or related compound. The destruction of accumulated acetylcholine can then proceed, and neuromuscular junctions will again function normally. Pralidoxime Chloride also slows the process of "aging" of phosphorylated cholinesterase to a nonreactivatable form, and detoxifies certain organophosphates by direct chemical reaction. The drug has its most critical effect in relieving paralysis of the muscles of respiration. Atropine is always required concomitantly to block the effect of accumulated acetylcholine at this site.

Mechanism of Action

Pralidoxime Chloride is an antidote to organophosphate pesticides and chemicals. Organophosphates bind to the esteratic site of acetylcholinesterase, which results initially in reversible inactivation of the enzyme. Acetylcholinesterase inhibition causes acetylcholine to accumulate in synapses, producing continuous stimulation of cholinergic fibers throughout the nervous systems. If given within 24 hours after organophosphate exposure, Pralidoxime Chloride reactivates the acetylcholinesterase by cleaving the phosphate-ester bond formed between the organophosphate and acetylcholinesterase.

Pharmacokinetic properties

Absorption: Animal studies suggest that the minimum therapeutic concentration of Pralidoxime Chloride in plasma is 4 µg/mL; this level is reached in about 16 minutes after a single injection of 600 mg Pralidoxime Chloride.

Distribution: Pralidoxime Chloride is distributed throughout the extracellular water; its apparent volume of distribution at steady state has been reported to range from 0.60 to 2.7 L/kg. Pralidoxime Chloride is not bound to plasma protein.

Metabolism: Pralidoxime Chloride is relatively short acting and repeated doses may be needed, unless continuous intravenous infusion is selected. Simulations suggest that after a dose of 1000 mg given intravenously, concentrations fall below 4 µg/mL in about 1.5 hours. The short duration of action of Pralidoxime Chloride and the necessity for repeated doses should be considered especially where there is any evidence of continuing absorption of the poison. The apparent half-life of Pralidoxime Chloride is 74 to 77 minutes.

Elimination: The drug is rapidly excreted in the urine partly unchanged and partly as a metabolite produced by the liver.

CLINICAL INFORMATION

Indications and Uses

Pradox is indicated as an antidote: (1) in the treatment of poisoning due to those pesticides and chemicals of the organophosphate class which have anticholinesterase activity and (2) in the control of overdosage by anticholinesterase drugs used in the treatment of myasthenia gravis.

Dosage and Administration

Adults: Inject an initial dose of 1000 to 2000 mg of Pradox (Pralidoxime Chloride), preferably as an infusion in 100 mL of normal saline, over a 15- to 30-minute period. If this is not practical or if pulmonary edema is present, the dose should be given slowly (over not less than five minutes) by intravenous injection, as a 50 mg/mL solution in water (e.g., 1000 mg in 20 mL). A second dose of 1000 to 2000 mg may be indicated after about one hour if muscle weakness has not been relieved. Additional doses may be given every 10-12 hours if muscle weakness persists.

Children ≤16 years: Loading dose: 20-50 mg/kg (maximum: 2000 mg/dose); Maintenance infusion: 10-20 mg/kg/hour; alternatively, a repeat bolus of 20-50 mg/kg (maximum: 2000 mg/dose) may be administered after 1 hour and repeated every 10-12 hours thereafter, as needed.

Children >16 years: Refer to adult dosing.

Preparation for Administration

Pradox (Pralidoxime Chloride) is supplied as 1000 mg single-dose vials for injection. For Intravenous infusion: Reconstitute a single Pradox (Pralidoxime Chloride) 1000 mg vial by adding 20 mL of Sterile Water for Injection, USP, which results in a 50 mg/mL concentration. The solution should be further diluted with Normal Saline for Injection, USP to achieve a concentration of 10 to 20 mg/mL (e.g. 1000 mg in 100 mL or 2000 mg in 100 mL). For fluid restricted patients or for rapid administration (over at least 5 min), a maximum concentration of 50 mg/mL may be used. Discard unused solution after a dose has been withdrawn.

Overdosage

Observed in normal subjects only: dizziness, blurred vision, diplopia, headache, impaired accommodation, nausea, slight tachycardia. Treatment of overdosage is artificial respiration and other supportive therapy should be administered as needed.

Use in Pregnancy and Lactation

Pregnancy Category C*;* Pralidoxime Chloride should be given to a pregnant woman only if clearly needed.

Contraindications

Pralidoxime Chloride is contraindicated in patients who are hypersensitive to any componant of the product.

Precaution

The following precautions should be kept in mind in the treatment of anticholinesterase poisoning, although they do not bear directly on the use of Pralidoxime Chloride, since barbiturates are potentiated by the anticholinesterases, they should be used cautiously in the treatment of convulsions; morphine, theophylline, aminophylline, succinylcholine, reserpine and phenothiazine-type tranquilizers should be avoided in patients with organophosphate poisoning. Prolonged paralysis has been reported in patients when succinylcholine is given with drugs having anticholinesterase activity; therefore, it should be used with caution.

Side Effects

Certain side effects, such as tachycardia, laryngospasm and muscle rigidity, have been attributed in a few cases to a too-rapid rate of injection.

Drug Interaction

When atropine and Pralidoxime Chloride are used together, the signs of atropinization (flushing, mydriasis, tachycardia, dryness of the mouth and nose) may occur earlier than might be expected when atropine is used alone. This is especially true if the total dose of atropine has been large and the administration of Pralidoxime Chloride has been delayed.

PHARMACEUTICAL INFORMATION

Storage condition

Store in a cool and dry place, away from light. Keep out of the reach of children.

Presentation & Packaging

Pradox Injection : Each commercial box contains 1 vial of Pralidoxime Chloride USP 1000 mg Injection (as lyophilized powder) and 2 ampoules of 10 ml Water for Injection.

Manufactured By

BEACON®

Pharmaceuticals PLC

Bhaluka, Mymensingh, Bangladesh

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