CITICOLINE

CALYXIN

500 mg Film-Coated Tablet

PSYCHOSTIMULANT / NOOTROPIC

FORMULATION:
Each film-coated contains:
Citicoline (as sodium) ..... 500 mg

PHARMACOLOGIC CATEGORY:
Psychostimulant / Nootropic

PRODUCT DESCRIPTION:
White colored oval film-coated tablet debossed with "CLM500" on one side.

PHARMACODYNAMICS/PHARMACOKINETICS:
Pharmacodynamics
Citicoline is a complex organic molecule that functions as an intermediate in the biosynthesis of cell embrane phospholipids. Citicoline is also known as CDP-choline or cytidine diphosphate choline (cystidine 5-'diphosphocholine). CDP-choline belongs to the group of biomolecules in living systems known as nucleotides that play important roles in cellular metabolism.
The pharmacologic action of citicoline appears to involve mechanisms that extend beyond phospholipid metabolism. Citicoline metabolites – choline, methionine, betaine, and cytidine-derived nucleotides – enter a number of metabolic pathways.
Biochemical markers of cholinergic nerve transmission are known to be deficient in conditions characterized by degeneration of cholinergic neurons, such as Alzheimer's disease. Citicoline modestly improves cognitive function in Alzheimer's disease by serving as an acetylcholine precursor. The brain uses choline preferentially for acetylcholine synthesis, which can limit the amount of choline available for phosphatidylcholine production.
Citicoline has been investigated as a therapy for stroke patients. Three mechanisms are postulated: (1) repair of the neural membrane via increased synthesis of phosphatidylcholine; (2) repair of damaged.
Cholinergic neurons via potentiation of acetylcholine production; and (3) reduction of free fatty acid build-up at the site of stroke-induced nerve damage.
Citicoline protects cholinergic neurons from auto cannibalism, a process in which membrane phospholipids are catabolized to provide choline for the synthesis of acetylcholine. This occurs when choline supplies are depleted, necessitating sacrifice of membrane phospholipids to maintain neurotransmission. As an exogenous source of choline for acetylcholine production, citicoline thus spares membrane phospholipids (in particular, phosphatidylcholine) and prevents neuronal cell death.
Pharmacokinetics
Citicoline is a water-soluble compound with greater than 90% bioavailability. Pharmacokinetic studies in healthy adults have shown oral doses of citicoline to be rapidly absorbed, with less than 1% excreted in the feces. Plasma levels peak in a biphasic manner, at 1 hour after ingestion followed by a second larger peak at 24 hours post dosing.
Citicoline is metabolized in the gut wall and liver. The byproducts of exogenous citicoline formed by hydrolysis in the internal wall are choline and cytidine. After absorption, choline and cytidine are dispersed throughout the body, enter systemic circulation for utilization in various biosynthetic pathways and cross the blood-brain barrier for resynthesis into citicoline in the brain.
Pharmacokinetic studies using ^{14}C citicoline show citicoline elimination occurs mainly via respiratory CO_2 and urinary excretion, in two phases, mirroring the biphasic plasma peaks. The initial peak in plasma concentration is followed by a sharp decline, which then slows over the next 4 to 10 hours. In the second phase, an initially rapid decline after the 24-hour plasma peak is similarly followed by a slower elimination rate. The elimination half-life is 56 hours for CO_2 and 71 hours for urinary excretion.

INDICATIONS:
- Acute and recovery phase of cerebral infarction (e.g. ischemia due to stroke)
- Cognitive dysfunction due to degenerative (i.e. Alzheimer's disease) and cerebrovascular disease
- Cerebral insufficiency (e.g. dizziness, memory loss, poor concentration, disorientation) due to head trauma or brain injury.
- Parkinson's disease

DOSAGE AND MODE OF ADMINISTRATION:
Dosing must be individualized and adjusted according to disease severity.
DOSE IN ADULTS (500 mg)
One tablet once or twice a day or as prescribed by the physician.

CONTRAINDICATIONS:
Hypersensitivity to any component of the product.
Patients with hypertonia of the parasympathetic nervous system

WARNINGS AND PRECAUTIONS:
Large doses of citicoline could aggravate increase in cerebral blood flow in episodes of persistent intracranial hemorrhage.

PREGNANCY AND LACTATION:
There is not enough evidence on citicoline's safety in pregnant and breastfeeding women. Citicoline should be used in pregnancy and breastfeeding only when benefits justify the potential risks.

INTERACTIONS:
Citicoline must not be administered with products containing meclofenoxate.
Citicoline potentiates the effects of L-dopa.

ADVERSE DRUG REACTIONS:
Cardiovascular: Bradycardia, tachycardia, hypotension
Gastrointestinal: Diarrhea, epigastric distress, stomach pain
Nervous: Dizziness, headache, fatigue
Skin: Rash

OVERDOSE AND TREATMENT:
Citicoline exhibits very low toxicity profile in humans. In clinical use it has been observed to be safe at doses up to 2g/day.

STORAGE CONDITIONS:
Store at temperatures not exceeding 30°C. Protect from light. Keep out of reach of children.

DOSAGE FORMS & PACKAGING AVAILABLE:
Dosage form: 500 mg Film-Coated Tablet
Packaging available: ALU-ALU Blister Pack by 10's; Box of 30's

CAUTION:
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

ADR REPORTING STATEMENT:
For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph

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