Citizac™

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Citicoline Tablets 500 mg

COMPOSITION
Each Film Coated Tablet Contains:
Citicoline Sodium
Eq. to Citicoline.....500 mg
Excipients q.s.
Colour: Titanium Dioxide BP

DESCRIPTION
CITIZAC™ contains Citicoline for the treatment of degenerative changes and chronic cerebral vascular injuries in senile dementia.

PHARMACODYNAMICS
Citicoline acts by various mechanisms as cerebral activator listed below:

Phospholipid Precursor
Evidence of citicoline's role as a phosphatidylcholine precursor has been found in animal studies. The brain uses choline preferentially for acetylcholine synthesis, which can limit the amount of choline available for phosphatidylcholine production. When the demand for acetylcholine increases or choline stores in the brain are low, phospholipids in the neuronal membrane can be catabolized to supply the needed choline. Exogenous citicoline thus helps preserve the structural and functional integrity of the neuronal membrane. In an in vitro study, citicoline at high concentrations stimulated brain acetylcholinesterase (AChE) along with Na+/K+-ATPase. The postulated mechanism involves bioconversion of citicoline to phosphatidylcholine.

Neuronal Membrane Repair
Citicoline has been investigated as a therapy for stroke patients. Three mechanisms are postulated: (1) repair of neuronal membranes via increased synthesis of phosphatidylcholine; (2) repair of damaged cholinergic neurons via potentiation of acetylcholine production; and (3) reduction of free fatty acid buildup at the site of stroke-induced nerve damage. In addition to phosphatidylcholine, citicoline serves as an intermediate in the synthesis of sphingomyelin, another neuronal membrane phospholipid component. Citicoline has shown the potential to restore post-ischemic sphingomyelin levels.
Citicoline also restores levels of cardiolipin, a phospholipid component of the inner mitochondrial membrane. The mechanism for this is unknown, but data suggest citicoline inhibits enzymatic hydrolysis of cardiolipin by phospholipase A2.11 In an animal study, citicoline decreased the formation of hydroxyl radicals following ischemia and perfusion, again suggesting citicoline acts to decrease phospholipase stimulation

Effect on Beta-Amyloid
Evidence has surfaced that citicoline counteracts the deposition of beta-amyloid, a neurotoxic protein believed to play a central role in the pathophysiology of Alzheimer's disease (AD). The characteristic lesion in AD is the formation of plaques and neurofibrillary tangles in the hippocampus. The degree of cognitive dysfunction and neurodegeneration in AD is proportional to the buildup of beta-amyloid. Citicoline counteracted neuronal degeneration in the rat hippocampus induced by intrahippocampal injection of beta-amyloid protein. The number of apoptotic cells was also reduced. Memory retention as measured by a passive-avoidance learning task improved in the rats.

Effect on Neurotransmitters
Evidence of citicoline's ability to enhance norepinephrine release in humans was found in a study showing citicoline raised urinary levels of 3-methoxy- 4-hydroxyphenylglycol (MHPG), a norepinephrine metabolite. Citicoline increased brain levels of neurotransmitters in rats at a dose of 100 mg/kg, administered daily for seven days. Norepinephrine increased in the cerebral cortex and hypothalamus; dopamine increased
in the corpus striatum, and serotonin increased in the cerebral cortex, striatum, and hypothalamus. Rat studies have found evidence that citicoline potentiates dopamine release in the brain, presumably by stimulating release of acetylcholine

PHARMACOKINETICS

Absorption
Citicoline is a water-soluble compound with greater than 90-percent bioavailability.

Distribution
Following 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 resynthesise into citicoline in the brain

Metabolism
Citicoline is metabolized in the gut wall and liver. The by-products of exogenous citicoline formed by hydrolysis in the intestinal wall are choline and cytidine

Excretion
Pharmacokinetic studies using 14C citicoline show citicoline elimination occurs in two phases mirroring the biphasic plasma peaks, mainly via respiratory CO2 and urinary excretion. The initial peak in plasma concentration is followed by a sharp decline, which then slows over the next 4-10 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 CO2 and 71 hours for urinary excretion.

THERAPEUTIC INDICATIONS
For the treatment of patients with serious cerebral injuries of vascular traumatic nature with or without loss of consciousness and for treatment of degenerative changes and chronic cerebral vascular injuries in senile dementia.

POSOLOGY AND METHOD OF ADMINISTRATION
Dosage should be individualized. The usually recommended dose of CITIZAC™ Tablet is 500–1,000 mg daily.
Take this medicine in the dose and duration as advised by your doctor. Swallow it as a whole. Do not chew, crush or break it. CITIZAC™ tablet may be taken with or without food, but it is better to take it at a fixed time.

Method of administration:
Oral administration

CONTRAINDICATION
Must not be administered to patients with hypertonic of the parasympathetic and hypersensitivity to citicoline or any other component of the formulation.

SPECIAL WARNING AND PRECAUTION FOR USE
Must not be administered in conjunction, with medications containing centrophenoxine. In case of persistent intracranial haemorrhage, it is recommended not to exceed the dose of 1000 mg daily.
Cholines are generally regarded as safe and appear to be well-tolerated. High intake of cholines may cause low blood pressure, steatorrhea (undigested fat in stool), nausea, vomiting, salivation, diarrhoea, constipation, anorexia, dizziness (vertigo), sweating, insomnia and headache. Cholines can possibly trigger existing epilepsy.
Dosages at the upper limit (UL) intake levels are contraindicated for person suffering from trimethylaminuria, Parkinson's disease, or kidney or liver disease. Skin rash has been reported. A cold and cough were noted in patients taking citicoline in a trial. Choline should be used cautiously by people with kidney or liver disorders. Agitation, paranoia and severe depression have been reported. Use cautiously in patients with a history of depression. Because choline is a product of the breakdown of succinylcholine, it may produce similar side effects as the drug, like respiratory depression. A "fishy" odour has been associated with choline. Sweating and stunted growth may occur.
Do not consume alcohol while taking citicoline. Make sure doctor is aware of upcoming surgeries that may have scheduled; or will be scheduling while taking this medication.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Levodopa
Citicoline may enhance the effects of levodopa. The exact mechanism is unknown, but animal models suggest that citicoline may increase dopamine levels in the brain and/or improve dopaminergic cell survival. In patients with Parkinson's disease, a few studies have demonstrated levodopa-saving effects, whereby the addition of citicoline (500 to 1200 mg/day) allowed for lower dosages of levodopa to be used with stable or improved therapeutic efficacy and reduced side effects in some patients. However, data are limited.

Coadministration with meclofenoxate
Citicoline must not be administered in conjunction with medication containing meclofenoxate (also known as Clophenoxate).

PREGNACY AND LACTATION

Pregnanacy
There are no adequate and well controlled studies of citicoline during pregnancy and lactation. Citicoline should be used in pregnancy only if the potential benefit justifies the potential risk to the foetus.

Breast-feeding
There are no adequate and well controlled studies of citicoline during pregnancy and lactation. Caution should be exercised during breastfeeding because it is not known whether citicoline is excreted in human breast milk.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
Citicoline may cause blurred vision and a decrease in blood pressure. So, it is recommended to be cautious to drive or operate heavy machinery after taking Citicoline.

UNDESIRABLE EFFECTS
Like all medicines, CITIZAC™ can cause side effects, although not everybody gets them. You may notice the following side effects:
- Anxiety
- Leg edema
- Agitation
- Constipation
- Dizziness
- Fever
- Headache
- Hematuria
- Hypotension
- Urinary tract infection
- Insomnia
- Joint pain
- Depression
- Auricular Fibrillation
- ECG abnormality

OVERDOSE
Citicoline exhibits very low toxicity profile in humans.

INCOMPATIBILITY
Not applicable.

SHELF LIFE
36 months

PACKAGING
10 Tablets are packed in Alu-Alu Blister and such 3 blisters are packed in a printed carton along with pack insert.

STORAGE CONDITION
Stored at a temperature not exceeding 30°C. Protect from light and moisture.
Keep the medicine out of reach of children.

Marketed by:

LINUX Laboratories Pvt. Ltd.
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