For the use of Registered Medical Practitioner of Hospital or a Laboratory only

Citicoline Injection 250mg/ml

COMPOSITION

Each ml contains

Citicoline Sodium Eq. to Citicoline		250 mg
Water for Injection	USP	q.s.

CLINICAL PHARMACOLOGY

Pharmacodynamic properties

When administered orally, it is absorbed almost completely, and its bioavailability is approximately the same when administered intravenously. Once absorbed, the cytidine and choline disperse widely throughout the body, cross the blood-brain barrier, and reach the central nervous system (CNS), where they are incorporated into the phospholipids fraction of the cellular membrane and microsomes. The concept that the administration of exogenous Citicoline can augment the synthesis of neural membrane phospholipids is attractive, because accelerated replacement or repair plays a critical role in maintaining the healthy function of numerous physiological processes. It has shown the therapeutic efficacy in a variety of diseases in which membrane disorder, dysfunction, or degeneration result in cellular and tissue ischaemia and necrosis.

Pharmacokinetic Properties

Absorption

Citicoline is well absorbed following intramuscular administration. After intramuscular doses of citicoline 1,000 mg, peak increases in plasma choline levels were seen in 0.4 hours, with levels increasing from 11 micromol/L (baseline) to 25 micromol/L

Distribution

Choline derived from citicoline crosses the blood–brain barrier, presumably serving as a source of acetylcholine and phosphatidylcholine (lecithin) synthesis. The major portion of a dose of citicoline appears to be incorporated into tissues and/or used in biosynthetic/ biodegradation pathways, including lecithin/lipid membrane synthesis.

Metabolism

Citicoline is metabolized in the liver to free choline. The liver is capable of synthesizing lecithin from choline. The half-life of free choline is of 2 hours after intramuscular administration.

Excretion

Only small amounts of dose are recovered in the urine and faeces (less than 3% each). Approximately 12% of a dose is eliminated through the lungs as carbon dioxide.

INDICATION AND USAGE

- Cerebrovascular diseases
- Head Trauma of varying severity
- Cognitive disorders of diverse aetiology
- Parkinson's disease

CONTRA-INDICATION

It must not be prescribed for patients with expressed vagotonia and hypersensitivity to any component.

In the absence of sufficient clinical data Citicoline solution for injection is not recommended for use in
children under 18 years.

DRUG INTERACTIONS

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).

WARNINGS AND PRECAUTIONS

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.

For patients with acute, severe and progressive disturbance of consciousness resulting from a head injury or brain operation, citicoline injection should be administered in conjunction with haemostatics and an intracranial pressure relieving drug, or a treatment such as hypothermia. For patients with disturbance of consciousness in the acute stage of cerebral infarction, it is recommended to start the administration of citicoline injection within 2 weeks after an apoplectic stroke.

In administering citicoline injection intramuscularly, caution should be exercised so as not to affect the tissues, nerves, etc. Intramuscular injection should be given only when indispensable and should be restricted to the minimum to be required. In particular, repeated injection at the same site should be avoided. Care should be exercised to avoid injection at sites along the course of the nerves. In case of intense pain or backflow of blood upon insertion of the injection needle, the needle should be withdrawn immediately and injected at a different site. In intravenous administration, inject as slowly as possible. Since shock may occur, a close observation should be maintained. If any such abnormalities such as drop in blood pressure, distressed feeling of the chest or dyspnoea are observed, citicoline injection should be discontinued and appropriate measures taken.

Persistent Intracranial Haemorrhage

In case of persistent intracranial haemorrhage, it is recommended not to exceed the dose of 1,000mg of citicoline daily, given through very slow intravenous administration (30 drops/minute)

SIDE EFFECTS

The commonly observed adverse effects (0.1–5%) with intravenous use of citicoline were rash, insomnia, occurrence or intensification of numbness of paralyzed extremities (when used in patients with post-apoplectic hemiplegia), nausea, abnormal laboratory values for function of the liver, and feeling of warmth. The other adverse reactions (<0.1%) were excitation, convulsions, anorexia, transient diplopia, transient blood pressure changes, malaise, shock, distressed feeling of the chest, and dyspnea. In a short-term, placebo-controlled, crossover study, 12 healthy adults took citicoline at daily doses of 600 mg and 1,000 mg or placebo for consecutive 5-day periods. Transient headaches occurred in 4 subjects on the 600 mg dose, 5 on the 1,000 mg dose, and 1 on placebo. No changes or abnormalities were observed in hematology, clinical biochemistry or neurological tests. A large drug surveillance study analyzed the results of citicoline treatment in 2,817 patients aged 60 to 80 years, suffering from senility and cerebral vascular insufficiency. A total of 151incidents of side effects were recorded, representing 5% of the patient sample. The most common adverse effects were transient in nature and included stomach pain and diarrhoea in 102 cases. Vascular symptoms of hypotension, tachycardia or bradycardia occurred in 16 cases.

Occasionally, citicoline may exert a stimulating action of the parasympathetic, as well as a fleeting and discrete hypotensive effect.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

As a result of the disease, the ability to drive and operate machinery may be impaired during treatment with Citicoline.

OVERDOSE

Citicoline exhibits very low toxicity profile in humans. In a short term, placebo controlled, crossover study, 12 healthy adults took citicoline at daily doses of 600 and 1000 mg or placebo consecutive 5-days periods. Transient headaches occurred in 4 subjects on 600 mg dose, 5 on the 1000 mg dose and 1 in placebo. No changes or abnormalities were observed.

DOSAGE & MODE OF ADMINISTRATION

Posology:

Disturbance of Consciousness resulting from head injury or brain operation

Usually for adults a dose of 500-1000 mg of CITICOLINE INJECTION Injection is administered once or twice a day, by intravenous drip, infusion, intravenous injection or intramuscular injection. The dose may be adjusted according to the patient's age and condition.

Disturbance of Consciousness in the Acute Stage of Cerebral Infarction

Usually, a dose of 1,000 mg of citicoline is administered once a day, by intravenous injection, for 2 consecutive weeks.

The dosage may be adjusted based on the seriousness of the disease. It can be administered intramuscularly, intravenously (3 to 5 minute) injection and in intravenous drop perfusion (dripping speed 40-60 drops/minute). Citicoline is compatible with all intravenous isotonic solutions. It can also be mixed with hypertonic glucose serum.

Method of administration: For I.V. or I.M. or I.V. drip infusion use only.

PREGNANCY AND LACTATION

There are no adequate and well controlled studies of citicoline during pregnancy and lactation. Citicoline should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Caution should be exercised during breastfeeding because it is not known whether citicoline is excreted in human breast milk.

STORAGE CONDITION

Store protected from light at a temperature not exceeding 25°C.

KEEP OUT OF REACH OF CHILDREN

PRESENTATION

2ml & 4ml Ampoule in cardboard carton along with pack insert.

MANUFACTURED IN INDIA

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