SUMMARY PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

CERAXON 1000 mg oral solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

CERAXON 1000 mg oral solution is supplied in sachets containing 10 ml of solution. Each ml contains 100 mg of citicoline (as sodium salt).

Excipients:
Per ml of solution: 2.5 mg of propyl parahydroxybenzoate; 14.5 mg of methyl parahydroxybenzoate; 2000 mg of sorbitol and other excipients in q.s.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral solution.

CERAXON 1000 mg oral solution: Sachets containing 10 ml of a transparent and white liquid with strawberry smell.

4. CLINICAL PARTICULARS

5. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Ischemic stroke, acute phase and its neurological sequelae (as a part of complex therapy)
- Rehabilitation period of ischemic and hemorrhagic stroke
- Traumatic Brain injury and its neurological sequelae, acute phase (as a part of complex therapy) and rehabilitation period
- Cognitive and behavioural impairment secondary to chronic vascular and degenerative cerebral disorders.

4.2 Posology and method of administration

Adults:

The recommended dose is from 500 to 2,000 mg/day, depending on the severity of the symptoms to be treated.

It may be taken directly or dissolved in half a glass of water (120 ml), with the meals or between them.

The dosage recommendations

The acute phase of Ischemic stroke and Traumatic Brain injury:

1000mg (10ml) every 12 hours. Treatment duration of at least 6 weeks.

Rehabilitation period of ischemic and hemorrhagic stroke, rehabilitation period of Traumatic Brain injury, Cognitive and behavioural impairment secondary to chronic vascular and degenerative cerebral disorders:

500-2000mg daily (5-10ml). The dosage and duration of treatment depend on the severity of symptoms.

See the instructions for preparation in section 6.6

Elderly:

CERAXON does not need any specific dose adjustment for this age group.

Children:

The experience in children is limited; therefore it may only be administered when the expected therapeutical benefit is higher than any possible risk.

4.3 Contraindications

- Hypersensitivity to any component
- Expressed vagotonia
- Rare inherited diseases associated with fructose intolerance
- Because of the absence of sufficient clinical data Ceraxon OS is not recommended for use in children under 18 years

4.4 Special Warnings and precautions for use

It is possible a formation of slight number of crystals in the cold, due to a temporary partial crystallization of preserving agent. With further storage under recommended conditions the crystals are dissolved in for several months. The presence of crystals does not affect the quality of the product.
In case of performing of potentially dangerous activities, requiring special attention and fast reactions the caution should be kept during the treatment.

4.5 Interaction with other medicinal products and other forms of interaction

Citicoline potentiates the effects of L-Dopa.

It must not be administered in conjunction with medicaments containing Meclofenoxate.

4.6 Pregnancy and lactation

There are no adequate data from the use of Citicoline in pregnant women.

CERAXON should not be used during pregnancy unless clearly necessary. That is, only when the expected therapeutic benefit is higher than any possible risk (see section 5.3).

If Citicoline is prescribed in lactation period, the breastfeeding must be stopped, as the allocation data of Citicoline with human milk are absent.

4.7 Effects on the ability to drive and use machines

CERAXON affects on the ability to drive and use of machines.

4.8 Undesirable effects

Very rare (<1/10,000) (include individual notifications)
Psychiatric disorders: hallucinations
Nervous system disorders: cephalea, vertigo, insomnia, excitation, sense of heat, numbness in paralyzed limbs
Vascular disorders: arterial hypertension, arterial hypotension
Respiratory, thoracic and mediastinal disorders: dyspnoea
Gastrointestinal disorders: nausea, vomiting, occasional diarrhea, anorexia, changes in the activity of hepatic enzymes
Skin and subcutaneous tissue disorders: blush, hives, exanthemas, purple
General disorders and administration site conditions: shiver, oedema

4.9 Overdose

No case of overdose has been reported

5. PHARMACOLOGOCAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Psychostimulants, agents used for Attention-Deficit Hyperactivity Disorder (ADHD) and nootropics.

ATC code: N06BX06

Citicoline stimulates the biosynthesis of structural phospholipids of the neuronal membrane as it is demonstrated in the magnetic resonance spectroscopy studies. Citicoline, through this action, improves the function of the membrane mechanisms, such as the functioning of the ionic exchange pumps and receptors inserted in the latter, the modulation of which is indispensable in the neurotransmission.

Citicoline due to its membrane stabilising activity has properties which favour brain oedema reabsorption.

Experimental studies have shown that Citicoline inhibits the activation of some phospholipases (A1, A2, C and D), reducing the formation of free radicals, avoiding the destruction of membranous systems and preserving antioxidant defence systems as glutation.

Citicoline preserves the neuronal energetic reserve, inhibits apoptosis and stimulates acetylcholine synthesis

It has been experimentally shown that Citicoline also exerts a prophylactic neuroprotective effect in focal brain ischemic models.

Clinical trials have shown that Citicoline significantly increases the functional evolution of patients with acute ischemic cerebrovascular accident, coinciding with a lower growth of the brain ischemic injury in neuroimagen tests.

In patients with craniocerebral traumatisms, citicoline speeds up their recuperation and reduces the duration and intensity of the post-concussional syndrome.

Citicoline improves the level of attention and consciousness and acts favourably over amnesia and cognitive and neurological disorders associated to brain ischemia.

5.2 Pharmacokinetic properties

Citicoline is well absorbed after oral, intramuscular or intravenous administration. Plasma choline levels significantly increase after the aforementioned routes. Oral absorption is nearly complete and its bioavailability is approximately the same as the intravenous route. The drug product is metabolized in the intestine and in the liver to choline and cytidine. The administered citicoline is widely distributed in brain structures, with a quick incorporation of the choline fraction in structural phospholipids and the cytidine fraction in cytidinic nucleotides and nucleic acids. Citicoline reaches the brain and it is actively incorporated to cellular, cytoplasmatic and mitochondrial membranes, taking part of the structural phospholipids fraction.

Only a small amount of the dose appears in urine and faeces (less than 3 %). Approximately 12 % of the dose is eliminated via expired CO_2. In the urinary excretion of the drug, two phases can be distinguished: a first phase, around 36 hours, where the excretion speed rapidly decreases, and a second phase where excretion speed decreases much slower. The same happens with expired CO_2, the elimination speed rapidly decreases after approximately 15 hours and later it decreases much slower.

5.3 Preclinical safety data

Oral and intraperitoneal chronic toxicity studies (1.5 g/kg/day during 6 months in dogs) did not show significant abnormalities related with the administration of the drug. Intravenous administration of 300-500 mg/kg/day of citicoline during 3 months in dogs, only produced toxic signs immediately after the injection, such as occasional vomiting, diarrhoea and hyper-salivation.

800 mg/kg of Citicoline was administered to albino rabbits during the organogenesis phase, from 7^{th} to 18^{th} gestation day. The animals were sacrificed the 29^{th} day and a detailed exam of foetus and their mothers was carried out. No toxicity sign were observed neither maternal nor embryo-foetal. The effects over organogenesis were inappreciable, only 10 % of the treated foetus has a slight delay in brain osteogenesis.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sorbitol 2000mg, Glycerol 500mg, Methyl parahydroxybenzoate 14,5mg, Propyl parahydroxybenzoate 2,5mg, Sodium citrate 60 mg, Sodium saccharin 2mg, Strawberry essence 4,08mg, Potassium sorbate 30mg, Citric acid 50% to pH 5,9-6,1 and Purified water to 10ml.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store not above 30° C.
Keep away from children.

6.5 Nature and contents of the container

Oral solution 100mg/ml.
Carton box with 6 or 10 sachets fastened two tear seam from combined material, containing 10 ml of solution each and instruction for use.

6.6 Special precautions for disposal and other handling

It may be taken directly from the sachet or dissolved in half a glass of water (120 ml).

6.7 MAH/Manufacturer:

Ferrer International, S.A.

Gran Via Carlos III, 94, 08028 Barcelona, Spain