# PROFESSIONAL INFORMATION

## SCHEDULING STATUS

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## 1 NAME OF THE MEDICINE

**CEBROLUX™ NF** powder for oral solution

Citicoline, multivitamin and mineral supplement

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

**Each 3 g sachet contains:**

Citicoline (Cognizin®) …….....250 mg

L-ascorbic acid (Vitamin C) ……..…60 mg

Niacin (Vitamin B3) ……..….12 mg NE*

Tocopherol (Vitamin E) …….8,2 mg α-TE**

Zinc (as citrate) …….6,25 mg

Pantothenic acid (Vitamin B5) ……. 4,5 mg

Pyridoxine (Vitamin B6) ……. 1,05 mg

Riboflavin (vitamin B2) ……. 1,05 mg

Thiamine (Vitamin B1) …….……...……. 0,83 mg

Retinol (Vitamin A) …….....…… 600 µg RE***

Folic acid (Vitamin B9) ……... 150 µg

Biotin (Vitamin H) ……. 37,5 µg

Cyanocobalamin (Vitamin B12) …… 1,875 µg

* NE = Niacin Equivalent, ** α- TE = α-Tocopherol Equivalent, ***RE = Retinol Equivalent

**Sugar free**

**Contains sweetener:** sucralose 20 mg/sachet

For full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Powder for oral solution.

CEBROLUX™ NF is a cream to light orange coloured powder with single red molecules.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

CEBROLUX™ NF is a multivitamin and mineral supplement containing a neuroprotective agent citicoline (Cognizin®). It is indicated in conditions where there is a reduced intake or increased need for these nutrients.

Nutrients in CEBROLUX™ NF contribute to:

- protection of cells from oxidative stress,
- normal synthesis and metabolism of some neurotransmitters,
- maintenance of normal vision,

- normal functioning of the nervous system, and
- normal cognitive function and mental performance.

### 4.2 Posology and method of administration

Take 1 to 2 sachets per day. Do not exceed the recommended daily intake.

- Dissolve the contents of a sachet in a glass of still water.
- Stir vigorously until the powder dissolves completely.
- Drink immediately after preparation. The prepared solution is yellow, with a citrus taste and smell.

**Paediatric population:** The safety and efficacy of CEBROLUX™ NF is children has not been established. No data are available.

### 4.3 Contraindications

Hypersensitivity to citicoline or any other ingredients (see **2 Qualitative and quantitative composition** and **6.1 List of excipients**).

### 4.4 Special warnings and precautions for use

A healthy lifestyle and a balanced diet are essential for staying in good health. CEBROLUX™ NF should not be used as a substitute for a varied diet.

CEBROLUX™ NF is intended only to complement health or supplement the diet, it is not intended as a substitute for medicine therapy.

**Paediatric population:** This product is intended only for adults.

### 4.5 Interaction with other medicines and other forms of interaction

No interaction studies have been performed.

### 4.6 Fertility, pregnancy and lactation

The safety of this preparation in pregnancy and lactation has not been established.

Pregnant and breastfeeding women should consult a doctor before use.

### 4.7 Effects on ability to drive and use machines

CEBROLUX™ NF is not expected to have a negative effect on the mental or physical ability to perform or execute tasks or activities requiring mental alertness, judgment or sound coordination and vision.

### 4.8 Undesirable effects

**a. Summary of the safety profile**

A medicine surveillance study analysed the results of citicoline treatment in more than 2 800 adults and found minor transient adverse effects in approximately 5 % of cases, most commonly stomach pain and diarrhoea.

**b. Tabulated summary of adverse reactions**

| | | |
|---|---|---|
| Vascular disorders | Uncommon (≥1/1 000 to <1/100) | Hypotension, tachycardia, bradycardia |
| Gastrointestinal disorders | Common (≥1/100 to <1/10) | Transient stomach pain and diarrhoea |

| | | |
|---|---|---|
| General disorders | Very common (≥1/10) | Transient headache |

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit-risk of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

Suspected adverse reactions may also be reported directly to the Applicant at the following e-mail address: PV-SouthAfrica@bauschhealth.com

### 4.9 Overdose

In overdose, side effects can be precipitated and/or be of increased severity. (See **4.8 Undesirable effects**)

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

D 34.12 Multiple substance formulation

- Citicoline, after oral administration, is hydrolysed by natural biochemical processes, supported by the vitamin B6, turning into choline, a molecule normally present in the human body. Choline is a natural precursor of the phospholipids involved in the formation and repair of neuronal membranes. Furthermore, choline is used by cells to

synthesize acetylcholine, a neurotransmitter essential for the propagation of the nerve signal.

- Choline, vitamins B2, C, E and zinc contribute to the protection of cells from oxidative stress.
- B vitamins, vitamin C and biotin contribute to normal functioning of the nervous system.
- Vitamins A, B2 and zinc contribute to the maintenance of normal vision.
- Choline and vitamin B5 contribute to normal mental performance, and the normal synthesis and metabolism of some neurotransmitters.
- Zinc contributes to normal cognitive function.

**5.2 Pharmacokinetic properties**

**Absorption:** Citicoline is a water-soluble compound with greater than 90 % bioavailability. Pharmacokinetic studies on healthy adults show oral doses of citicoline are rapidly absorbed, with less than 1 % excreted in faeces. Plasma levels peak in a biphasic manner, at one hour after ingestion followed by a second larger peak at 24 hours post-dosing.

**Metabolism:** Citicoline is metabolised in the gut wall and liver. The by-products of exogenous citicoline formed by hydrolysis in the intestinal wall are choline and cytidine. 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 re-synthesis into citicoline in the brain.

**Elimination:** Pharmacokinetic studies using C citicoline show citicoline elimination occurs in two phases mirroring the biphasic plasma peaks, mainly via respiratory $CO_2$ 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 21-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.

**5.3 Preclinical safety data**

Citicoline has been found to have a very low toxicity profile in toxicology studies in animals and humans.

The $LD_{50}$ of a single intravenous dose of citicoline is 4 600 mg/kg and 4 150 mg/kg in mice and rats, respectively. An oral $LD_{50}$ could not be determined as no deaths occurred at the maximum possible oral dose.

No toxic effects were observed in 30 day sub-acute toxicity studies of oral citicoline to 2 groups of rats at doses of 100 mg/kg and 150 mg/kg. no changes occurred in blood chemistry, organ histology, or urinary parameters.

The effect of chronic oral consumption of citicoline was studied in dogs fed a single 1,5 g/kg dose daily for six months. No toxic effects were seen nor did any physiological, biochemical, neurological, or morphological abnormalities occur.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Beta carotene (E160)

Citric acid

Lime flavour

Maltodextrin

Silicon dioxide

Sucralose (sweetener)

## 6.2 Incompatibilities

Not applicable

## 6.3 Shelf life

2 years

## 6.4 Special precautions for storage

Store in a dry place, below 25 °C.

## 6.5 Nature and contents of container

CEBROLUX$^{TM}$ NF is provided in aluminium foil sachets containing 3 g of powder per sachet.

A unit carton contains either 30 sachets or 5 sachets.

### 6.6 Special precautions for disposal

No special requirements.

## 7 APPLICANT

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## 8 REGISTRATION NUMBER

Not registered

**Complementary Medicine: Health Supplement**

This unregistered medicine has not been evaluated by the SAHPRA for its quality, safety or intended use.

## 9 DATE OF REVISION OF THE TEXT

April 2021