1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

Gamalate B_6 coated tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each coated tablet contains:
- magnesium glutamate hydrobromide (MGH) ..... 75 mg
- γ-amino-butyric acid (GABA) ..... 75 mg
- γ-amino β-hydroxybutyric acid (GABOB) ..... 37 mg
- Pyridoxine hydrochloride ..... 37 mg

3. PHARMACEUTICAL FORM

Coated tablet

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Gamalate B_6 belongs to the group of drugs called psychostimulants and nootropics.
Gamalate B_6 owing to the action of its active components: cerebrotonic aminoacids (GABA and GABOB), mild sedative (MGH) and vitamin B_6, exerts a cerebral energizing and neuroregulating action. The aminoacids and vitamin B_6 take part in the cerebral metabolism and increase the energetic potential of the nervous cell. It improves the output of the intellectual qualities.

Indications
Adjuvant in functional asthenias:
- Emotional instability.
- Concentration and memory difficulty.
- Depression and nervous breakdown.
- Decreased adaptation capacity.

4.2 Posology and method of administration

Posology
Adults: 2 tablets, 2 or 3 times a day (every 12 or 8 hours).
Pediatric population (over 7 years): 2 tablets, 2 or 3 times a day (every 12 or 8 hours).

These dose recommendations may be modified by the doctor.

4.3 Method of administration

This medicinal product is administered by oral route. May be administered before or after main meals.

4.4 Contraindications

Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.

4.5 Special warnings and precautions for use

Not known.

4.6 Pediatric population

Not known.

4.7 Interaction with other medicinal products and other forms of interaction

Not known.

4.8 Additional information on special populations

Not applicable

4.9 Paediatric population

Gamalate B_6 coated tablet can be administered to pediatric population (over 7 years).

4.10 Fertility, pregnancy and lactation

If required by the case, administer it under medical vigilance.

4.11 Effects on ability to drive and use machines

Not known.

4.12 Undesirable effects

At the maximum doses, it may produce slight gastric disorders which disappear on adjusting the dose.

4.13 Overdose

Given the scarce toxicity of the preparation the appearance of symptoms of poisoning is highly unlikely.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Psychoanaleptics. Other psychostimulant and nootropic drugs.
ATC Code: N06BX.

γ-amino-butyric acid (GABA) arises from glutamic acid through the action of the enzyme glutamate decarboxylase (GAD) and mainly inhibits neural excitatory activity. It is metabolised in the brain by transamination and decarboxylation and transformed into succinic acid and

incorporated into the Krebs Cycle. The factors affecting GABA content or conditions in the brain have a notable influence on cerebral activities. The GABA level depends on the activity of the decarboxylase in the glutamic acid formed by GABA, and the transaminase that GABA eliminates. Disorders on a synaptic transmission level are detected in situations of overexcitement. In these circumstances the enzyme levels required for the transformation of glutamic acid into GABA are reduced and so glutamic acid and GABA levels, which are the two main amino acid neurotransmitters.

γ-amino-β-hydroxy-butyric acid (GABOB) is a natural metabolic product and structural precursor analogue of GABA that has neuro-modulating properties in the brain. It blocks excitatory synaptic terminals and modulates dopaminergic and GABAergic activity.

α-Amino magnesium glutamate hydrobromide (MGH) is a synthetic molecule. The main structural core of MGH is glutamic acid. It has been demonstrated that it exerts a mild sedative effect with anxiolytic activity due to its chemical structure. It acts as a partial agonist of L-glutamate, blocking its excitatory action.

Pyridoxine hydrochloride (vitamin B_6) is a water-soluble vitamin involved in the transformation of glutamic acid into GABA. It is essential for normal functioning of the Central Nervous System (CNS) and acts as a coenzyme factor in many neuronal processes.

The pharmacologic action of Gamalate B_6 is based on the complementary action of the four components which increase the energy potential of the nerve cell and on their sedative action on hyperexcitability, which provides a better concentration and mental performance. Each of the ingredients contained in acts to maintain the physiological homeostasis of the CNS, and the aim of combined administration is to potentiate these effects in cases where this homeostasis is disrupted. GABA in Gamalate B_6 ensures correct GABA concentrations in the CNS and normalises the biochemical processes involved in its metabolic production, at synaptic level, in hyperexcited neuronal states; GABOB enhances the GABA inhibitory function in the CNS; MGH helps reducing glutamate-mediated excitation in the CNS by blocking its receptors, and vitamin B_6 stimulates the metabolic conversion of glutamate to GABA, thus enhancing its activity.

5.2 Pharmacokinetic properties

Gamalate B_6 is well absorbed by oral route.

GABA is absorbed rapidly and crosses the blood-brain barrier. It is metabolised into succinic acid by a process of transamination and decarboxylation for incorporation into the Krebs Cycle. Alternatively, GABA is metabolised into GABOB.

GABOB has rapid oral absorption and can cross the blood-brain barrier. It is extensively metabolised and rapidly eliminated in urine and saliva. Only about 1% of the dose is recovered in urine and is detected at 12 hours, thus proving an extensive metabolism.

After oral absorption, MGH passes into the blood stream, with wide systemic distribution.

Pyridoxine hydrochloride is rapidly absorbed in the gastrointestinal tract. The absorption is reduced in patients with malabsorption syndrome. It does not bind to plasma proteins. Its reservoir is the liver where it transforms into active pyridoxal 5'-phosphate and pyridoxamine phosphate coenzymes. It undergoes hepatic metabolism by oxidation giving rise to 4-pyridoxic

acid and other inactive metabolites that are eliminated in urine. Its elimination half-life is 15-20 days. It can be eliminated by haemodialysis. Pyridoxine crosses the placenta and is excreted in breast milk.

5.3 Preclinical safety data

The LD_{50} of Gamalate B_6 coated tablets was determined in albino rats weighing 20-25 g by administering solution in distilled water through gastric cannula. A single dose of 5 g/Kg had no effect either in mortality nor external toxicity symptons inmediately and during 24, 48 and 72 hours after the administration. Being that the maximum dose administered corresponding to 22g/Kg of the medicine and so the LD_{50} in this animal model can be considered undeterminable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose, Anhydrous colloidal silica, polyvinylpyrrolidone (E-1201), Sodium starch glycolate, Magnesium stearate, Talc (E-553b), Maize starch, Titanium dioxide (E-171), Magnesium carbonate (E-504i), Indigotine (E-132), Eudragit E, Gum arabic (E414), Propylene glycol (E-1520) and Carnauba wax (E-903).

6.2 Incompatibilities

Not applicable.

6.3 Shelf-life

5 years.

6.4 Special precautions for storage

Store below 30ºC.

6.5 Nature and contents of the container

Blue round tablets, packed into blisters.
It contains 20 and 60 coated tablets.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

7. MARKETING AUTHORISATION HOLDER AND MANFUACTURING SITE

Ferrer Internacional, S.A.
Head Office:
Gran Vía Carlos III, 94
08028 Barcelona (Spain)

Production site:
Joan Buscallà, 1-9
08173 Sant Cugat del Vallès
Barcelona (Spain)

8. MARKETING AUTHORISATION NUMBER

9. DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION

10. DATE OF REVISION OF THE TEXT