1. NAME OF THE MEDICINAL PRODUCT

Gamalate B_6 oral solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 100 ml of oral solution contains:
- magnesium glutamate hydrobromide (MGH) ..... 2 g
- γ-amino-butyric acid (GABA) ..... 2 g
- γ-amino β-hydroxybutyric acid (GABOB) ..... 1 g
- Pyridoxine hydrochloride ..... 1 g

Excipient(s) with known effect
Sorbitol 70% (E-420); Sunset Yellow FCF (E-110); methyl para-hydroxybenzoate (E-218); Sodium propyl parahydroxybenzoate (E-216).
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORMULATION

Oral solution

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

Children:
- Concentration difficulty and decreased school output.
- Lack of adaptation to social, family and school milieu.

4.2 Dosage and method of administration

Posology
Adults and children over 7 years: 10 ml 2 or 3 times a day (every 12 or 8 hours).
Children up to 2 years: 2.5 ml 3 times a day (every 8 hours).
From 2-4 years: 5 ml 3 times a day (every 8 hours).
From 4-7 years: 10 ml 2 times a day (every 12 hours).

These dose recommendations may be modified by the doctor.

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

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Warning about excipients:
This medicinal product contains sorbitol. Patients with hereditary intolerance to fructose should not take this medicinal product. It may produce a mild laxative effect because it contains 3 g of sorbitol per 5 ml.

This medicinal product may cause allergic reactions because it contains Sunset Yellow FCF (E-110). It may cause asthma, especially in patients allergic to acetylsalicylic acid.

It may cause allergic reactions (possibly tardive) because it contains methyl para-hydroxybenzoate (E-218) and propyl para-hydroxybenzoate (E-216).

4.5 Interaction with other medicinal products and other forms of interaction

Not known.

4.6 Pregnancy and lactation

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

4.7 Effects on ability to drive or operate machinery

Not relevant.

4.8 Adverse reactions

The adverse reactions are classified by organs, systems and frequencies, using the following MedDRA convention for frequency: Very common (≥1/10), Common (≥1/100 a <1/10), Uncommon (≥1/1,000 a <1/100), Rare (≥1/10,000 a <1/1,000), Very rare (<1/10,000), unknown frequency (cannot be estimated from the data available).

System organ class	**Frequency**
	Very rare (<1/10,000)
Nervous system disorders:	Drowsiness, sedation, disorientation, extrapyramidal reactions.
Respiratory, thoracic, and mediastinal disorders:	Dyspnoea, bronchospasm.
Gastrointestinal disorders:	Nausea, vomiting, occasional diarrhoea, xerostomia, constipation, jaundice, cholestasis.
Skin and subcutaneous tissue disorders:	Rubor, urticaria, erythema, purpura, eczema.

4.9 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 oral solution 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 oral solution 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 Pre-clinical safety data

The DL_{50} of Gamalate B_6 oral solution was determined in albino Wistar rats weighing 180-220 g by administering a 12% solution in distilled water through gastric cannula. Only one death was recorded in 24 hours with the maximum dose administered of 6 g/Kg and corresponding to 100 cc of solution per kilogram and so the DL_{50} in this animal model can be considered undeterminable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium saccharin; citric acid; methyl para-hydroxybenzoate (E-218); Sodium propyl parahydroxybenzoate (E-216); raspberry essence; Sunset Yellow FCF (E-110); sorbitol (E-420) and purified water.

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

Amber coloured glass flask with screw cap containing 80 ml of de oral solution.

6.6 Special instructions for disposal

No special requirements for disposal.

7. MARKETING AUTHORISATION HOLDER

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

8. FINISHED PRODUCT MANUFACTURER

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